THE American Journal OF Gastroenterology

VOL. 22, NO. 4 OCTOBER, 1954

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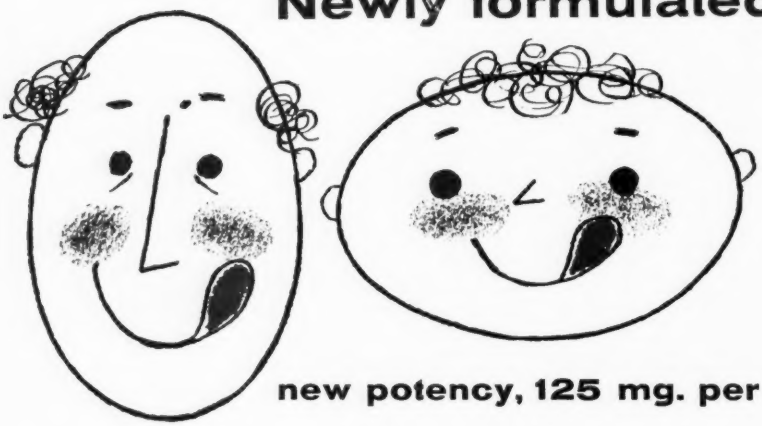

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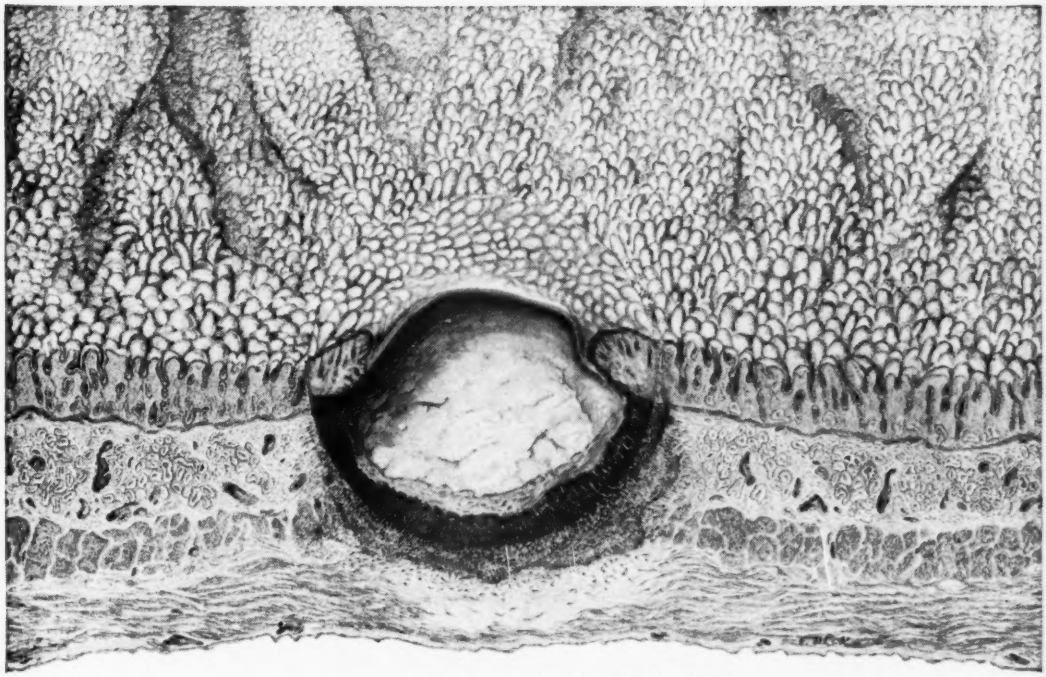

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contents:

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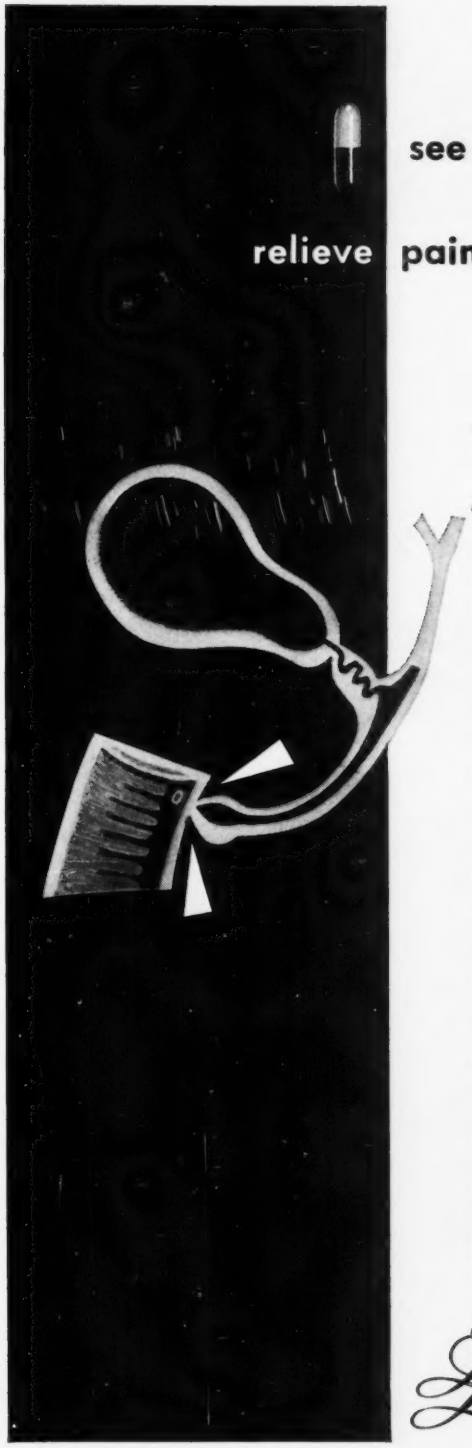

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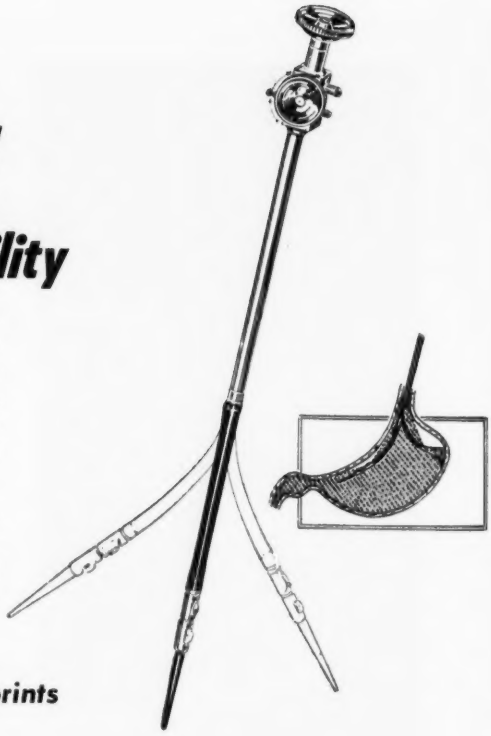

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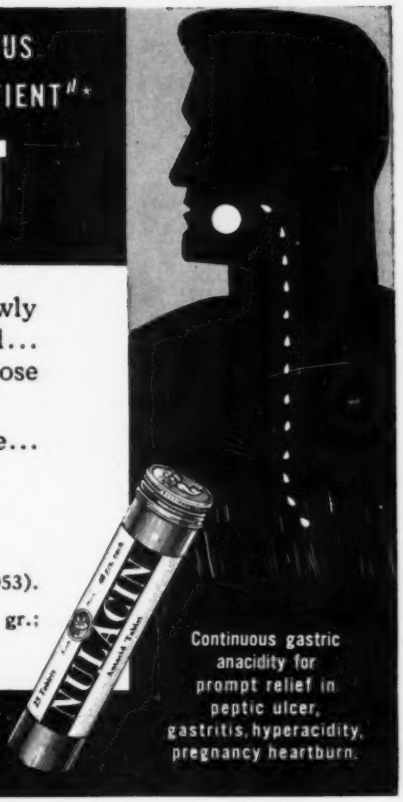

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POSTGASTRECTOMY AND POSTANASTOMOTIC SYNDROMES*†

M. E. STEINBERG, M.D.

Portland, Oreg.

Based on the interpretation of disabling symptoms in 30 patients subjected to corrective surgery and aided by concepts scanned from the literature, it is warranted to place certain postgrastrectomy and postanastomotic symptoms and disturbances into one or another niche in the following design of syndromes.

1. *Reflux Syndrome* (Schindler; Steinberg; Wells and Welbourn)
   a. Afferent loop stasis with reflux (Steinberg, 1940; Wells and Welbourn, 1951, 1952).
   b. Afferent loop stasis without bilious vomiting (Figs. 1a, 1b, 1c).
   c. Pendulum reflex (Steinberg) (Figs. 1d and 1e).
   d. Uncomplicated isoperistaltic afferent loop reflux (Steinberg). This mechanism is most frequently observed in connection with a wide gastrojejunal stoma as is found in Polya technic (Figs. 1f and 1g).
   e. Reflux with malfunction at the efferent angle of the stoma or efferent jejunal loop (Figs. 1h, 1i and 1j).
   f. Cup-and-spill mechanism, which is occasionally observed in patients with large gastric pouches (Figure 1k).
   g. Combination of the above mechanisms of reflux.
2. *Gastric Pouch Syndrome*
3. *Dumping* (Efferent loop syndrome; Wells and Welbourn, 1951)
4. *Combination of Syndromes*

REFLUX SYNDROME

Under the reflux syndrome are included a variety of mechanisms which affect the entrance of irritating doudenal contents into the gastric pouch and

*Presented before the Course in Postgraduate Gastroenterology of the National Gastroenterological Association, Los Angeles Calif., 15, 16, 17 October 1953.

†Part of this study was supported by a United States Public Health Service Grant-in-Aid.

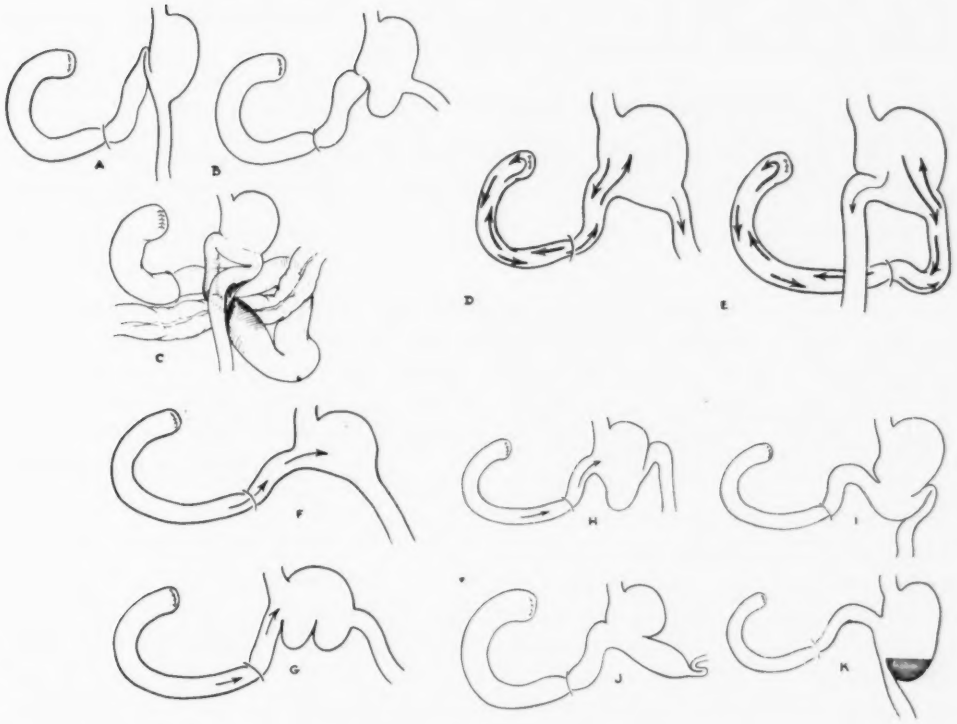
From the Department of Physiology, University of Oregon Medical School and from the Emanuel Hospital, Portland, Oreg.

into the esophagus with or without malfunction at either the afferent or efferent areas around the anastomosis. Conditions prevailing in the presence of either the afferent or the efferent loop stasis with reflux will manfest symptoms and disabilities frequently different and at times of more concern to the patient than simple reflux without stasis. Several mechanisms causing reflux and stasis may co-exist. The above arrangement is mostly based on personal experience with corrective surgery for postgastrectomy and postanastomotic side-effects. It is apparent that there are other mechanisms which may cause malfunction.

I first called attention in 1940 to the deleterious effects from reflux of bile and pancreatic juice into the gastric pouch. "The presence of bile and pancreatic juice which may stagnate in the stomach may be a positive factor in gastritis and of some of the dyspeptic symptoms. Stagnation in the proximal jejunal loop or duodenum should also be considered as probable cause of dyspepsia"[13].

Afferent loop stasis with reflux is caused by partial obstruction from kinks, tortions or adhesions proximal to the gastroenteric stoma (Figs. 1a, 1b and 1c). Wells and Welbourn (1951) recognized malfunction from stasis in the proximal enteric segment and designated this syndrome as "afferent loop stasis with reflux". Accumulation of enteric secretions in the afferent loop raises the intramural pressure resulting in a peristaltic rush of biliary and pancreatic contents either into the gastric pouch or into the efferent jejunal loop.

Certain types of gastrojejunal anastomosis favor the entrance of ingested foodstuffs into the proximal enteric segment by gravity. Such placement of a gastrojejunal stoma, particularly when the stoma is wide, also favors the entrance of biliary and pancreatic secretions into the gastric pouch. One can follow the see-saw movements of a barium swallow between the proximal enteric gut and the gastric pouch. I designated this mechanism as "pendulum reflux" (Figs. 1d and 1e). Some consider that the to-and-fro pendulum-like movement of the gastric contents between the proximal gut and the gastric pouch is desirable (Smedal and Conlon). Benefits in digestion which may accrue from such churning mechanisms are likely to be annulled by distress from gastritis, vomiting and esophagitis. In the pantaloon type of gastrectomy such churning and mixing of foodstuffs with digestive juices may be considered as beneficial and may not be productive of any side-effects because the duodenal contents seldom enter into the gastric pouch in large amounts (Fig. 2b). Any of the reflux mechanisms may initiate a crop of distressing symptoms and disabilities which may simulate, aggravate, merge or overlap with those which comprise disturbances originating either in the gastric pouch syndrome or in the efferent loop syndrome (dumping). Diarrhea, steatorrhea, nausea, vomiting, malnutrition and numerous postgastrectomy disturbances may be the symptoms and disabilities resultant from any of the postgastrectomy syndromes. Roentgenograms depicting an antecholic Polya type of gastrectomy with the jejunal loop directed from left to right frequently shows a heavier shadow in the proximal jejunal loop. Such roentgenograms are considered as not depicting anything abnormal. This type



Figs. 1a, b and c—Afferent loop stasis with reflux. a. Kinking of the afferent jejunal loop on the lesser curvature. b. Partial stenosis at the afferent angle of the stoma. c. Antecholic anastomosis with compression of afferent jejunal loop by the jejunal mesentery. Similar mechanism may cause acute obstruction. Partial obstruction may also result from the compression of the jejunal loops riding on a distended transverse colon.

Figs. 1d and e—Pendulum reflux. d. Pendulum reflux in a Reichle-Polya anastomosis with the proximal jejunal loop from right to left. e. Pendulum reflux is more commonly observed in an antecholic gastrectomy with the jejunal loop directed from left to right.

Figs. 1f and g—Uncomplicated isoperistaltic reflux. f. Reichle-Polya anastomosis with a wide stoma. g. Same as f with redundancy and double sacculation of jejunal wall opposite the stoma.

Figs. 1h, i, j and k—Reflux complicated by efferent loop stasis. h. High attachment of distal jejunum on the greater curvature with a jejunal sacculation opposite stoma. i. Kinking of distal jejunal loop from adhesions of the loop to the jejunal segment opposite the stoma. j. Kinking of distal jejunal loop some distance from the stoma. k. Reflux with "cup-and-spill" mechanism. This is most frequently seen in gastrectomies with large gastric pouches. This mechanism is erroneously recommended to forestall dumping. Malfunction with stasis at the efferent loop may result from the pressure of the sac along the greater curvature on the efferent jejunal loop.

of operation in several of our patients was responsible for serious symptoms from vomiting and anorexia. Yet, there was no evidence of malfunction in the sense of an afferent or efferent loop stasis. It is for this reason that this type of reflux deserves a separate designation (Pendulum Reflux).

Case Histories of Patients with Pendulum Reflux

Case 3:—A farmer, age 26, was subjected to a Polya antecholic gastrectomy with the jejunal loop directed from left to right for an ulcer. He began to have

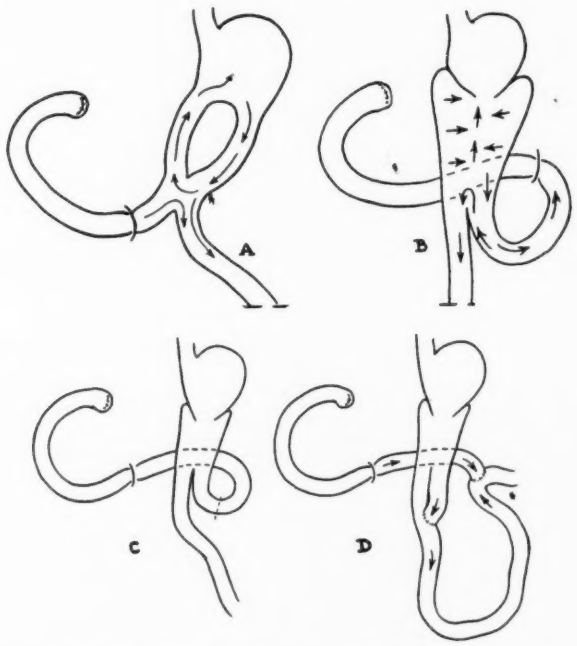


Fig. 2a—Braun enteroenteroanastomosis will rarely forestall reflux unless the afferent enteric loop is considerably dilated in the presence of obstruction.

Fig. 2b—Pantaloon anastomosis in the presence of an efficient valve is more likely to preclude reflux. Partial benefits in digestion may be postulated from churning and mixing of foodstuffs in the jejunal pouch.

Fig. 2c—Diagram of a completed pantaloon anastomosis which failed to relieve serious disabilities from reflux in two patients.

Fig. 2d—Y anastomosis of Roux relieved both patients of reflux. The distal stoma of the severed jejunal loop emerging from the jejunal pouch has not been closed but anastomosed to the distal jejunal pouch. This was done to avoid a blind sac.

persisting vomitings of bile and was unable to eat. He lost 47 pounds in weight in 4 months. The roentgenogram showed the usual picture of a resected stomach with precipitous emptying of a conventional barium meal (Fig. 3d). The patient was unable to eat and was sustained on intravenous feedings for six days prior

to surgery. A pantaloon type of gastrectomy was performed on April 4, 1949. The patient made an excellent immediate recovery and began to take nourisment on the third postoperative day. He now eats about as much at one time as he did before his first operation. He gained over 50 pounds in weight. He does a long day's work on his farm.

It is evident that in spite of the precipitate emptying of the barium swallow the disabling symptoms were not to be attributed to the dumping syndrome but to gastritis and to loss of bile and pancreatic juice. This was clearly an example of a pendulum reflux mechanism resulting in crippling disabilities and with a grim prognosis.

Case 9:—A farmer, age 26, was subjected to a Hofmeister-Finsterer retrocolic gastrectomy for duodenal ulcer on May 12, 1946. The patient had frequent vomitings of bile and hematemesis. He was admitted to the hospital on May 12, 1947 with a hemoglobin reading of 32 per cent. An additional part of gastric tissue was removed and a vagotomy was performed on May 17, 1947 for a penetrating jejunal ulcer.

The patient stopped bleeding but soon began to complain of frequent vomitings of bile and also of food. He filled up with gas and vomited about a pint of bile, particularly after he went to bed. Later in the night he woke up two or three times and brought up a half a cup of bile. He was not able to sleep unless his head was elevated. The bile burned his mouth and palate which frequently became swollen so that he was unable to eat. He would feel better if he would vomit every hour. Eggs, cream, cereals, toast and sweets made him vomit. He was unable to eat at breakfast time until he had taken from 7 to 10 cups of tea. He usually drank about 30 cups of tea during the day which seemed to give him some relief from the bile. He lost about 40 pounds in weight.

The roentgen examination showed a small gastric pouch with the barium shadow in the afferent and efferent loops and without any evidence of malfunction. He was subjected to a pantaloon gastrectomy on August 3, 1950. This patient made an excellent recovery. He is now able to sleep in a reclined position. He has gained 34 pounds in weight. He now tolerates cakes, pies, cereals and cream. He is not, however, able to tolerate large meals at one time but eats about five meals daily without any discomfort. There is no vomiting. He works long hours as a laborer in a lumber mill.

This is clearly a case which demonstrates intractable postgrastrectomy side-effects resultant from either an isoperistaltic or a pendulum reflux mechanism.

Pain in the right hypochondrium and in the back, a feeling of pressure and nausea are symptomatic of the afferent loop stasis mechanism with or without reflux. Most frequently smaller or larger amounts of bile-stained fluid is usually vomited between meals. Some patients state that they may partake of a substantial meal and yet vomit about a half to a glassful or unbelievable large

amounts of pure bile about ten to fifteen minutes after eating. Apparently the rapid evacuation of food stimulates peristalsis in a partially occluded afferent loop. Relief is obtained immediately after the vomiting. In the presence of any of the reflux mechanisms, when the gastric pouch is minimal, bile-stained vomitus frequently comes shortly after a meal and may be mixed with food. A number of patients complained of anorexia at breakfast time. This meal may be the only

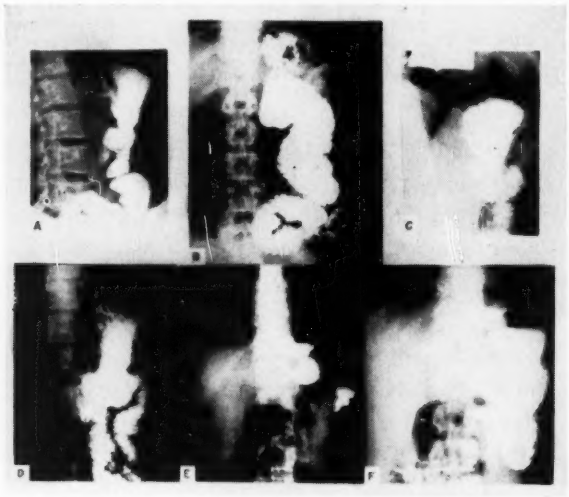


Fig. 3a—(Case 1). Roentgenogram of a conventional Hofmeister-Finsterer retrocolic gastrectomy with no evidence of malfunction. Grave and intractable postgastrectomy side-effects from simple reflux and dumping.

Fig. 3b—(Case 1). Postoperative roentgenogram of Case 1 in a. Only fleeting retention of barium seen in a minimal gastric pouch. Heavy barium shadow seen in a large jejunal pouch. Patient made a complete recovery.

Fig. 3c—(Case 2). Roentgenogram of a conventional retrocolic Hofmeister-Finsterer gastrectomy. No barium shadow is observed in the jejunal loop proximal to the ligament of Treitz. Grave and lasting postgastrectomy side-effects pointing to an afferent loop stasis with reflux and dumping. Complete relief after corrective surgery by pantaloon anastomosis.

Fig. 3d—(Case 3). Typical textbook picture of an antecholic Polya gastrectomy with afferent jejunal loop directed from the greater to the lesser curvature. Such a roentgenogram is not considered abnormal. This patient has had alarmingly grave postgastrectomy disabilities from bilious vomiting and inability to eat. This is a typical pendulum reflux mechanism. Complete rehabilitation with gain of over 50 pounds after corrective surgery by pantaloon anastomosis.

Fig. 3e—(Case 4). Roentgenogram of an antecholic Reichle-Polya gastrectomy with a minimal gastric pouch. Lower shadow apparently represents barium in an enteroenteroanastomosis which was the third operation in this patient and intended to forestall reflux. Severe postgastrectomy symptoms from reflux in spite of the enteroenteroanastomosis. Possible afferent and also efferent mechanisms of stasis because no barium shadow is seen either in the afferent nor efferent loops. Roentgenogram after pantaloon anastomosis in Case 4 sent in by the patient. Satisfactory result. Complete relief from reflux.

one causing the distress. Such patients avoid eating for several hours usually until either mid-morning or noon. One of my patients was in the habit of drinking from 7 to 10 cups of tea in the morning before he was able to tolerate any type of food. After the corrective operation by the pantaloon anastomosis his morning anorexia completely vanished, and he also stopped partaking of tea on arising. Another patient reported that she was procuring carbonated drinks by the case. She cleared her stomach of bile by drinking several bottles of carbonated drinks before she could partake of any food. The recumbent position during the night favors the entrance of duodenal contents into the gastric pouch causing temporary edema and inflammation which apparently partially subside after a few hours when the patient assumes the upright position. Some patients also complain of a bitter taste in their mouth which they frequently speak of as "acid". Others complain of sore throats and some are able to sleep in a propped-up position only.

Clay-colored stools, steatorrhea and diarrhea occurred in several of our patients from vomiting of copious amounts of bile-stained fluid. The diarrhea frequently occurred after a large vomitus of bile. The frequency of bowel movements, pasty stools and steatorrhea may be occasioned by the loss of large amount of pancreatic juice and bile to vomiting and because of the rapid passage of food from the gastric pouch which remains unmixed with such duodenal juices which are still left and which may either precede or follow the rapid passage of food. Patients with diarrhea and steatorrhea were cured after the corrective operation by the pantaloon anastomosis. Some patients, instead of having diarrheal stools, became constipated and had to resort to laxatives. An elderly school teacher was subjected to three unsuccessful operations and never ceased to vomit bile-stained contents until after I performed a Roux anastomosis. She volunteered that she lost her feeling of fatigue and lassitude a few days after the Roux operation when she ceased vomiting bile-stained contents. She felt stronger than in all years during which she was continuously vomiting. It is reasonable to assume that her electrolyte balance was re-established when she ceased losing the duodenal contents.

Case Histories of Patients with Afferent Loop Stasis, with Gastric Pouch Syndrome and with Dumping

The disturbances in these patients were symptomatic of the whole gamut of syndromes.

Case 11:—A male laborer, age 55, underwent a gastroenterostomy for a duodenal ulcer in 1922. He had several episodes of hematemesis, bilious vomiting and nausea. He underwent a subtotal gastrectomy by the Hofmeister technic for a jejunal ulcer in 1939. This patient has never been well since his first operation in 1922. After the Finsterer retrocolic gastrectomy he began to complain of persistent pain under the right costal margin which usually awakened him regularly at about 4 or 5 o'clock in the morning. The pain lasted until he started moving. He then immediately began to pass copious amounts of clear urine

every 15 minutes for one hour or longer. He also brings up large quantities of bile-stained vomitus which gives him relief. He does not tolerate his breakfast. Lunch makes him nauseated and he breaks out in cold perspiration. He becomes shaky and weak and hot water breaks out on his lips. He is not able to tolerate ice-cream, milk, pork chops, salad, ham, onions, etc. He lost more than 20 pounds in weight. The roentgenogram showed no barium shadow in the afferent enteric loop. A pantaloon anastomosis was done on June 18, 1951. The patient has never had any vomiting spells since the operation. He feels much better and can tolerate foods which he was unable to eat before. He no longer awakens in the

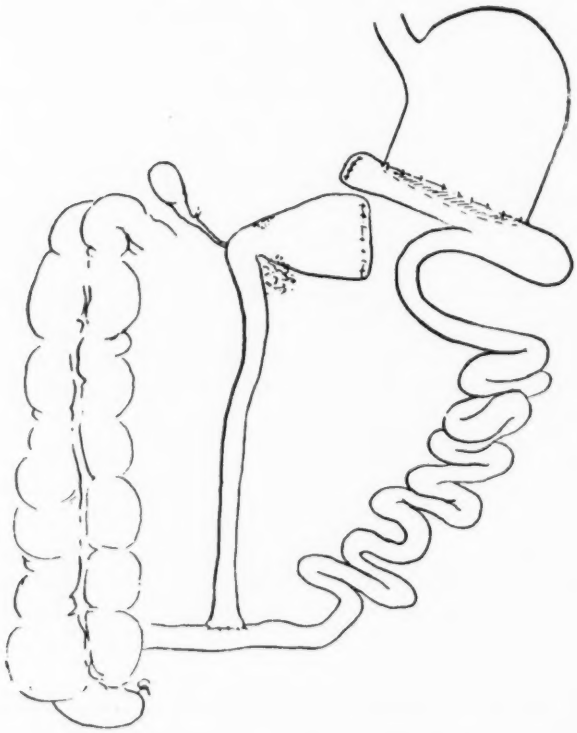


Fig. 4—Enteroenteroanastomosis opposite the gastric stoma. First presented by Steinberg and Starr, *Arch. Surg.*, December, 1934. This was the forerunner of the technic presently employed in the pantaloon method of anastomosis.

morning with pain in the right upper quadrant. He gained 12 pounds in weight and he is well satisfied with the result of the operation.

This patient's most troublesome symptoms after the first conventional gastrectomy can best be interpreted on the basis of an afferent loop stasis with reflux and on the dumping syndrome. Apparently the pantaloon anastomosis not only relieved the serious symptoms from afferent loop stasis but also ameliorated symptoms characteristic of dumping.

Case 4:—A physician, age 38, was subjected to a subtotal gastrectomy for duodenal ulcer in 1946. He lost about 50 pounds in weight in 6 months and had frequent bowel movements. The x-ray revealed a gastroileostomy. In January, 1947, the anastomosis was taken down and an additional part of gastric tissue removed. The gastrojejunal continuity was then reestablished antecholic with a Hofmeister valve. He began to have severe postprandial symptoms immediately after the second gastrectomy. Six months later he was operated for intestinal obstruction. Because of bilious vomiting an enteroenteroanastomosis was performed between the proximal and distal jejunal loops distal to the gastrojejunal anastomosis (Fig. 2a). This operation brought no relief from bilious vomiting. The patient was first seen on December 8, 1950. He complained of weakness,

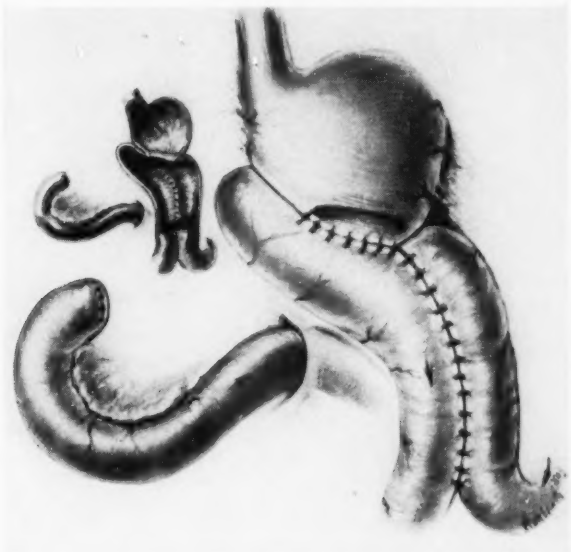


Fig. 5—Diagram of a completed pantaloon anastomosis. Variations in the technic have been used.

nausea, perspiration which started either during the meal or immediately after. There is an increase in the pulse rate and a feeling of extreme weakness as of a mild form of shock. He obtained some relief after lying down for 30 to 60 minutes. Such annoying and distressing postprandial attacks are brought on by all foods particularly milk, milk shakes, ice cream and soups. He vomits bile about once a week. If the vomiting comes immediately after eating it usually consists of food. He also gets occasional attacks of weakness which he ascribes to hypoglycemia. His weight before the operation was 175 pounds. His present weight is 120 pounds. He is unable to attend to his professional duties.

The patient was operated on December 16, 1950. The gastric remnant measured no more than about 3 cm. along the greater curvature side. The antecholic anastomosis was dismantled and a long pantaloon anastomosis made

joining the previous enteroenteroanastomosis. This created a very large jejunal pouch. Because of the minimal capacity of the gastric pouch no attempt was made to form a gastrojejunal valve.

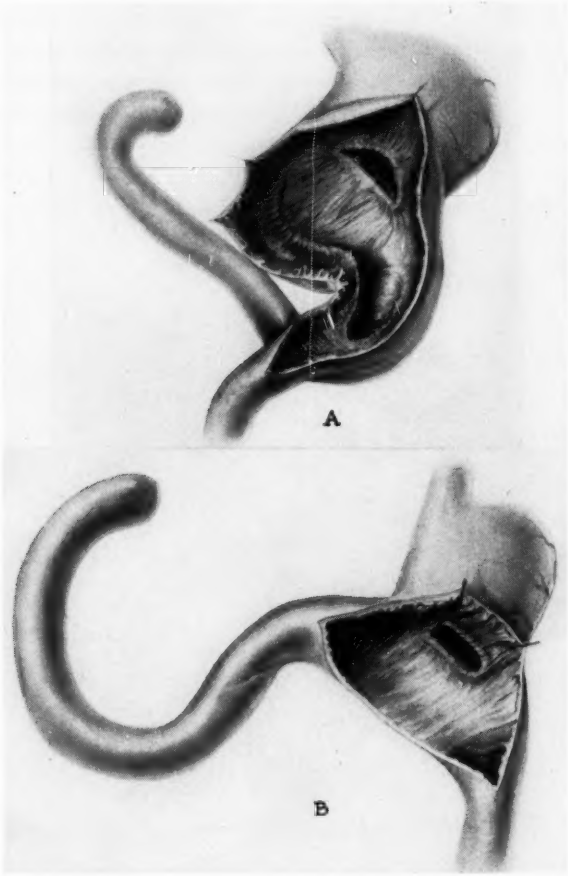


Fig. 6a—Postmortem specimen of a pantaloon anastomosis. Patient was operated for a large gastric ulcer. Patient was a dipsomaniac. Death occurred four months after the operation from an overdose of barbiturates. Anatomical capacity of jejunal pouch comparable to that of the gastric pouch.

Fig. 6b—Postmortem specimen of a Hofmeister-Finsterer retrocolic conventional gastrectomy. This patient was also a dipsomaniac operated many years ago because of an hour-glass stenosis of the stomach from ingestion of hydrochloric acid in an attempt at suicide. This patient also died years later from an overdose of barbiturates.

This patient, who was despairing and unable to attend to his professional duties is now busily engaged in the practice of medicine. He tolerates all foods with the exception of soups. He has gained more than 20 pounds in weight and he is well satisfied with the result of the operation. From a personal communication, "I benefited wonderfully well by the operation".

In this patient there was a kinking in the afferent loop from the pressure of the colon on the emerging jejunal loops. The symptoms pointed to the whole gamut of a postgastrectomy syndrome. The pantaloon operation relieved reflux and ameliorated some of the manifestations of the gastric pouch and the dumping syndrome. The patient states that he is not able to tolerate soups. It is noteworthy to observe that the long enteroenteroanastomosis which was done in

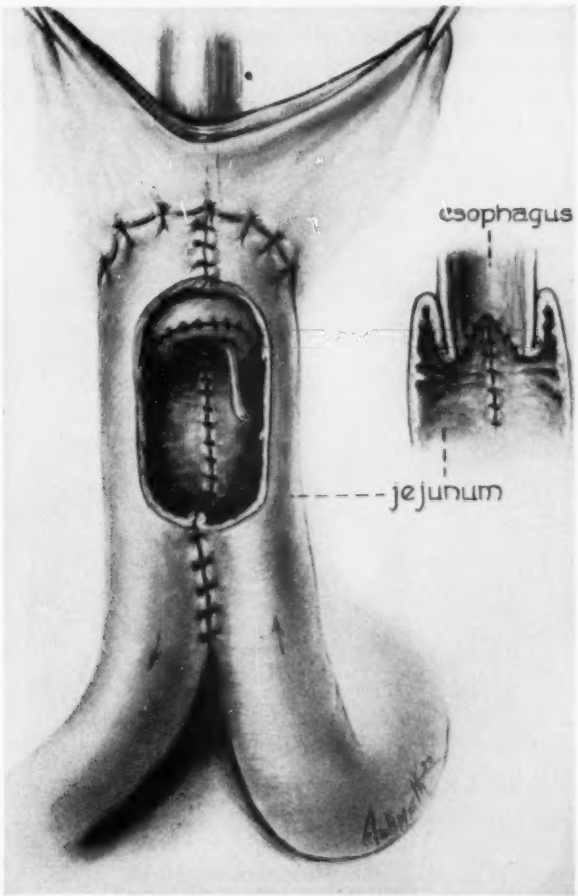


Fig. 7—Technic of a total gastrectomy by the pantaloon method. An efficient valve is important to prevent reflux. The jejunal pouch is now fashioned much longer for total gastrectomies than is depicted in this illustration.

order to forestall reflux into the gastric pouch did not bring any relief from vomiting.

Case 5:—A physician, age 52, had a gastroenterostomy done for a duodenal ulcer in 1927. Because of unabated and unendurable postprandial discomfort with nausea and continuous tasting of bile he consulted another surgeon in 1931 who dismantled the gastroenterostomy and performed a plyoroplasty.

The patient was relieved of his nausea and was able to tolerate such foods as milk, meat, desserts and eggs which had made him ill after the gastroenterostomy. He began to develop symptoms from retention and consulted a third surgeon in 1947 who advised a gastrectomy. Immediately after the gastrectomy the patient became wretched because of a continuous nauseating feeling. Vomiting of bile caused a fearful irritation in his mouth which lasted for hours. The nausea was particularly annoying after meals. He was partially relieved of the nausea after he remained quiet and after lying down for half an hour after meals. The tasting of bile was relieved after drinking ice water or Coca-Cola. The epigastric distress and nausea was worse during the night. He used to break out in a sweat with

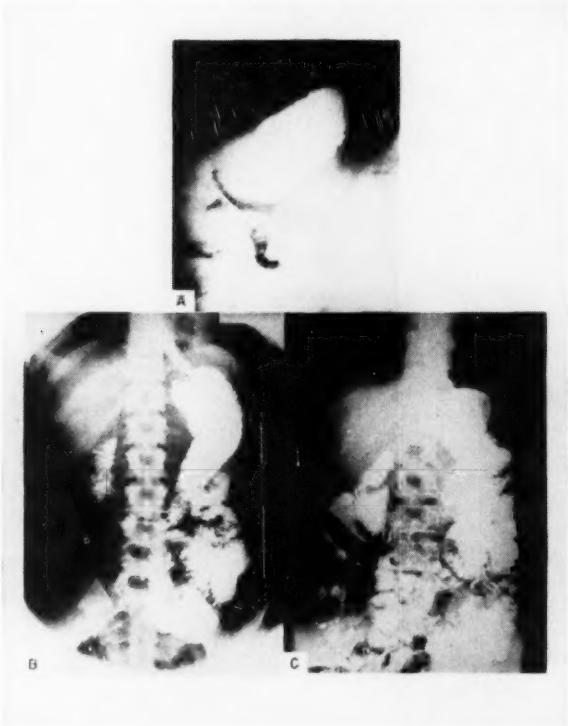


Fig. 8—Roentgenograms of esophagojejunal anastomoses by the pantaloon technic after total gastrectomies.

a rapid pulse and experienced a faint feeling immediately after eating. All of these postprandial symptoms are now somewhat abated. He also gets occasional spells of exhausting weakness betwen meals which is relieved by food. The patient states that if he had been aware that such unabating distress and annoying symptoms were to follow the gastrectomy operation, he would have rather suffered disabilities from retention and got along on soft and liquid foods. The x-ray disclosed a gastric resection with a gastrojejunostomy. The afferent jejunal loop at the lesser curvature side was about 5 cm. higher than the emerging distal jejunal loop at the greater curvature side. There is no barium

shadow in the afferent loop. The emptying was slow with formation of fluid and gas levels above the barium level.

A pantaloon anastomosis was performed on February 21, 1952. The proximal jejunal loop was found to be kinked where the previous jejunal stoma from the gastroenterostomy had been closed. The proximal jejunal loop was also found to be attached high on the lesser curvature near the esophagus. There was no evidence of dysfunction in the distal jejunal loop.

The patient now tolerates his food well. He is not nauseated and has resumed his surgical practice. He recently met with an accident which resulted in a fractured spine, and he did not suffer from any annoyances during the course of his illness and the convalescence that followed. The patient is well satisfied with the result of the operation. In a personal communication he states, "Really, it is so wonderful to feel human again".

From the roentgenogram and the symptoms it is warranted to assume that the patient's difficulties were due to an afferent loop stasis with reflux.

Four patients have experienced repeated vomitings of blood mixed with biliary contents. No jejunal ulcers were demonstrated, and since no acid was found in the gastric contents after repeated stimulation by histamine, it may be inferred that the hemorrhages were due to gastritis from tryptic digestion. In these patients, as in several others with reflux syndromes, the mucosa of the terminal part of the gastric pouch was found swollen and had the appearance of hemorrhoidal tissue.

The deleterious results from regurgitation of pancreatic juice and bile entering the gastric pouch had not received deserved attention in the consideration of postgastrectomy disturbances. Excessive reflux of enteric contents into the gastric lumen or esophagus is frequently the only major disability in the gastrectomized patient. Gastroscopic examination of the stomach after the various modifications of Billroth I or II operations frequently reveal some form of gastritis. During the examination one sees foamy intestinal contents constantly pouring into the gastric pouch.

Schindler was the first to describe the frequency of severe gastritis in the postoperative stomach. He concludes thus, "The unregulating reflux of intestinal juices through the stoma is the chief reason for the origin of chronic inflammation of the postoperative stomach, and the operations which do not prevent this reflux cannot be considered the proper treatment for any benign disease such as peptic ulcer". Schindler also states that the symptoms of postoperative gastritis are characterized by torturing continuity and intractability. "There is a certain unanimity of opinion that the treatment of gastritis of the postoperative stomach is one of the most hopeless tasks." Most frequently one can obtain biliary contents by gastric aspiration in gastrectomized patients with no apparent evidence of any disturbances resulting from the presence of biliary contents entering the

gastric pouch. Apparently, the fleeting presence of limited amounts of duodenal contents either in the intact stomach or in the gastric pouch evokes no demonstrable symptoms or disabilities. In the gastric pouch the presence of bile and pancreatic juice in time result in atrophic gastritis which, as a late manifestation, may even be considered as a welcome process since it results either in reduction of acid secretion or in achylia (Boller). It must be inferred that it is only when severe forms of gastritis are present with swollen and livid gastric folds and esophagitis with nausea and vomiting and loss of duodenal contents, diarrhea and steatorrhea that simple isoperistaltic or pendulum reflux gains in importance as a definitive factor in postgastrectomy difficulties. In the presence of a small gastric pouch the cardia frequently remains open permitting reflux of duodenal contents into the esophagus. More distress can be anticipated with a similar quantity of reflux in a smaller than in a larger pouch. Patients have been observed who were painfully and continuously distressed with unabating nausea and with no vomiting. Apparently the nausea was the result of severe gastritis and esophagitis. These patients were cured after corrective surgery by the pantaloon operation. The following case histories demonstrate that reflux is a distinct and crippling entity which may follow either the Billroth I or the Billroth II operations.

Case 20:—A housewife, age 48, with a history of neurosis and an irritable bowel, constipation and insomnia, was subjected to a gastrectomy on April 13, 1951 for a gastric ulcer. The gastroenteric continuity was established by the Billroth I end-to-end method. She immediately began to complain of nausea, particularly after breakfast. There was a pressure in the epigastrium with a nauseated feeling in the throat. She was continuously belching and had bilious vomitings three or four times daily. Occasionally there was some food in the vomitus. The Billroth I anastomosis was taken down and a pantaloon anastomosis was done on September 29, 1951. The bilious vomiting, anorexia and postprandial distress returned with the same severity as after the Billroth I operation. The third operation was done on October 30, 1952. A kink in the jejunal pouch was corrected. The gastrojejunal stoma was made smaller and the valve effect enhanced. The result of the third operation was equally disappointing with bilious vomiting and nausea returning. Because of such unabating and distressing symptoms surgery was performed for the fourth time on May 7, 1953. The gallbladder, which showed definite signs of inflammation, was removed. The jejunal pouch was not disturbed. A modified Roux anastomosis was made (Figs. 2c and d). This patient has not vomited since the Roux anastomosis. She eats well, looks much better but is still constipated and is unable to sleep.

Case 21:—This is another example of serious disabilities caused from reflux. A woman school teacher, age 67, was subjected to pyloroplasty and a cholecystectomy and appendectomy in 1937. A conventional gastrectomy was done in 1950 presumably for an obstructive duodenal ulcer. She began to have bilious vomiting two or three times a day and was getting up every night to drain the

bile out of her stomach. She was unable to tolerate eggs, meat, milk and fats of any kind. She was continously tired, weak and languid. She lost 45 pounds in weight. A pantaloon anastomosis was done on July 3, 1951.

I was painfully surprised when I received the following letter: "The operation did not do what we had hoped. It is a year of dragging, miserable existence. It is a terrible disappointment to find that the thing it was to do for me is still not done. I am up three to four times a night to draw up about a pint of clear bile fluid. When I get up in the morning I drain my stomach of yellow, liquid like this (she inserted a line with a light yellow colored pencil to indicate the color of the bile). Sometimes it is a little darker. I think all of the bile kicks back into the stomach. I sometimes wonder if there is a restriction in the tubes where they empty into the intestines. I can feel it labor often before it kicks back into the stomach. The bile builds up and there is a warning for several hours before the bile comes. I buy "7-up" by the case. This year of dragging, weak and almost helpless condition is something too rugged to face without apprehension." This letter is inserted because it portrays a typical story symptomatic of reflux syndrome with stasis. It is related by the patient herself without prompting of any kind or interrogation.

I performed surgery for the second time on May 26, 1953. I did not wish to risk another disappointment by simply enhancing the gastrojejunal valve. I, therefore, performed a Roux anastomosis (Figs. 2c and d). The patient made an immediate and excellent recovery. She has not felt like this in years and she never thought that she could regain so much strength in such a short time. She always has been tired and weak. Nothing disagrees with her at the present time and she can tolerate bacon, meat, potatoes, gravy and all other foods "with the rest of them". She does not fill up any more and can go to bed with a full stomach. After the previous operation she had to empty her stomach before she could go to sleep. She gained 17 pounds in a short period of time. The weakness and fatigue that this patient had before the duodenal contents were side-tracked were apparently the result from the loss of electrolytes through vomiting. The symptoms here were indicative of an afferent loop stasis with reflux which were unrelieved by the pantaloon anastomosis.

Gastric Pouch Syndrome

Because of a small gastric pouch there is reduced capacity for storage and churning and also reduced intake of food. The loss of acid and pepsin can cause an interference with the absorption of iron and vitamins. Bacteria from the lower regions of the small bowel and from the large bowel find a favorable habitat in the proximal small bowel and in the gastric pouch. Megaloblastic anemia, which has been predicted for the gastrectomized patient, has not been realized (Boller). Apparently the intrinsic factor left in the fundus is sufficient for hemopoiesis. Alteration of function and resulting disabilities from sacrifice of gastric tissue are closely related and interdependent with dislocations

of normal functions also brought about by any artifically made gastroenteric continuity. An indefinite though considerable number of patients are unable to partake of a heavy meal because of a feeling of fullness, nausea and vomiting. Several patients have stated that an extra mouthful of food after a meal would bring on perfuse perspiration, nausea and vomiting. According to Capper and Butler[3], vasomotor upsets such as feeling of warmth, sweating and tachycardia and palpitation were not reproduced by distention of the jejunum but completely reproduced by inert substances such as barium or mercury in the gastric remnant with the patient in the upright position. These authors conclude that the weight of the contents in the gastric pouch plus the weight of the contents in the afferent loop are complementary factors in the production of this syndrome. Only the sensation of abdominal fullness was reproduced by distention of the jejunum. Capper and Butler conclude "dumping is due to the drag on the gastric stump". Capper reports that the reconstruction of the supports to the gastric pouch has been successful in 8 of the 9 cases with "early postgastrectomy syndromes". In an earlier publication it was suggested that postcibal symptoms are not all resultant from dumping but that some of these are due to distention of the gastric pouch (Steinberg[13]). It is, however, unlikely that a gastric pouch or the intact stomach can be freed from drag and be prevented from becoming distended by some sort of fixation. Operations for visceroptotic stomachs have proved disappointing. Wells and MacPhee[11] suggest that improvement in postgastrectomy disabilities after corrective operations by fixation reported by Capper and Butler[3] was in all likelihood brought about by a change in the gastrojejunal relationship at the stoma, thus mitigating the afferent loop stasis with reflux.

Efferent Loop Syndrome (Dumping)

When the symptoms are considered to originate in the efferent jejunal loop Wells and Welbourn describe the condition as the "efferent loop syndrome"[12].

The mechanism involved in certain postcibal symptoms, the deficiency in the utilization and absorption of certain foods, the inability to gain in weight, intolerance to certain foods, diarrhea, steatorrhea, hypoglycemia, etc., are related to the loss of gastric functions and to the rapid entrance and transit of large quantities of unprepared foods into the efferent loops of the small bowel. Adlersberg and Hammerschlag introduced a term "early postprandial symptoms" as distinguished from "late postprandial symptoms". From the following discussion it is obvious that some early postprandial symptoms apply not only to the dumping mechanism but also to the reflux and to the gastric pouch syndrome.

Early Postprandial Symptoms:—Soon after a meal the patient may complain of drowsiness, fullness, nausea, eructation and flushing of the face. The feeling of lassitude and a sense of warmth together with belching and beads of perspiration may simulate an attack of syncopy. Early postprandial symptoms vary in intensity. At first the patient may be greatly alarmed, but he soon learns that

if he assumes the recumbent position the symptoms usually disappear rather suddenly after some minutes to an hour. It is claimed that the relief given by recumbency is due to the slowing of evacuation from the gastric pouch. It may also be assumed that symptoms caused by disturbances in vasomotor equilibrium and by cerebral ischemia because of a splanchnic overflow of blood are ameliorated after the patient assumes a recumbent position. The above symptoms together with intolerance of some foods, such as milk, pastry and concentrated carbohydrates, have not had a satisfactory explanation. Although such disturbances are considered to originate from dumping of foodstuffs into the jejunum, it is not always evident which symptoms originate because of the small capacity of the gastric pouch and which are due to dumping. Some patients have been known to tolerate rich desserts on an empty stomach but not after a meal. I have also knowledge of three patients with total gastrectomies and with a pantaloon method of esophagojejunal anastomosis who were free of some of the postcibal side-effects ascribed to dumping. One of these patients who, has not succumbed to her malignancy, partakes of large quantities of foods at one sitting and tolerates milk, pastries, etc., without annoyances. It is considered that intolerance to certain foods may also indicate an allergic phenomenon due to absorption of incompletely broken down proteins (Boller). Distention of the jejunum by outpouring of excessive jejunal secretions, caused by the presence of hypertonic foodstuffs, has been advanced as the cause for some of the symptoms due to dumping (Machella)[4]. Others have considered the early postprandial symptoms from dumping in the nature of a splanchnic or vasomotor disturbance initiated by some sort of a neurovisceral reflex. Spasm of the jejunum from a sudden insult of foodstuffs of high osmotic pressure may cause reverse peristalsis and should also be considered as one of the factors in the dumping mechanism causing nausea and vomiting. According to Wells and MacPhee[11] increased tension in the jejunum with hyperperistalsis rather than distention is the mechanism of the efferent loop syndrome. The entrance of large quantities of intestinal gas into the gastric pouch after a meal is to be considered as the component of the dumping mechanism (Boller). On certain occasions, when the patient is examined under the fluoroscope, gas from the small intestinal loops is seen to enter the gastric pouch and to elevate the left diaphragm. The patient complains of distress and anxiety, less common of a rapid heart beat, and with pain under the sternum. The patient may become alarmed complaining of nausea and retching without ability to vomit. The patient learns that his discomfort can be relieved by belching or by massage in the region of the epigastrium or by assuming a recumbent position. The gas belched up by the patients frequently has a putrid odor. According to Boller the relief which is obtained after the belching makes it possible to recognize this mechanism from the other components of the efferent loop syndrome or from the gastric pouch syndrome. Two of my patients were in the habit of massaging the abdomen particularly in the right upper quadrant in order to bring up large quantities of gas for relief. It may well be that this belched-up gas was entrapped in the partially occluded

proximal enteric segment (afferent loop stasis). It may be assumed that in the presence of an afferent loop stasis the barium swallow initiates a peristaltic rush in the semiclosed afferent loop which brings on the distress described by Boller.

Bowel unrest and colic is frequently observed after total gastrectomy and after partial gastrectomy, particularly in psychoneurotic individuals. Diarrhea and steatorrhea are considered to be caused by jejunitis, altered bacterial flora, lack of fat absorption, increase of intestinal motility and failure of the food to be thoroughly mixed with the bile and pancreatic juice. Pale stools, diarrhea and steatorrhea as a component of the reflux syndrome have been discussed in previous pages.

A fall in serum potassium during dumping attacks has recently been demonstrated by W. Hamilton Smith.

Loss of weight, malnutrition, macrocytic anemia, vitamin deficiencies may be common to the efferent loop syndrome and also to the reflux and gastric pouch syndromes.

The late postprandial symptoms because of dumping take place between meals when the gastric pouch is empty. The patient complains of weakness, palpitation, trembling, shortness of breath and a flickering before the eyes. Such symptoms may be rushed in with an alarming swiftness and end in syncopy. One of my patients was jailed by police because they thought that he was inebriated when they found him unconscious on the sidewalk. Another of my patients found unconscious was taken to a hospital and given saline infusion. The incidence of the late postprandial symptoms, in my experience, have been uncommon. The hypoglycemia syndrome is more commonly observed in psychoneurotics and asthenic individuals as are also the other symptoms from dumping.

Hypoglycemia, after an initially elevated circulating blood sugar from rapid absorption from the intestines, appeared as a possible explanation for the syndrome because of an increased insulin secretion. J. B. Butler[2] submits with caution that evidence obtained from his studies indicate that the cause of the syndrome may be temporary inhibition of glycogenolysis in the liver in response to high degrees of portal hypoglycemia due to rapid absorption of carbohydrates.

Case history of a patient with serious disturbances symptomatic of the dumping syndrome:

Case 22:—The pantaloon operation failed miserably in a woman 47-years old. This patient was well, had a good appetite, and worked hard until about four years before she was first subjected to a gastrectomy. Her complaints were headache, nervousness and continual belching. Ice cream and soft drinks made her ill. She lost 30 pounds in weight because eating caused pain. She was treated for her various ailments then finally was subjected to a minimal gastrectomy presumably for some kind of an ulcer. Her abdominal pain and discomfort became

continuous. "You can see the intestines roll". "Water goes right through the intestines". Any food now makes her ill. She vomits "green stuff". Headache is continuous and unbearable, particularly right after eating. She weighed 120 pounds in 1947. Her present is 97 pounds. She passes a great deal of mucus with her stools. She is unable to sleep and takes barbiturates and occasionally opiates. This was a pathetically haggard and emaciated looking individual. She was subjected to a modified pantaloon anastomosis with the purpose of fashioning a valve to slow down her gastric evacuation. She stopped vomiting bile, but all of the other symptoms returned with a violent fury. She began to notice blood and more mucus in her stools. It is apparent that dumping aggravated her previous symptoms and added some new ones. She consulted other physicians and clinics and finally came to see me because she was advised elsewhere that another operation would bring relief. I have not been able to get in touch with this patient after I advised her and her husband that observation would be necessary before I could advise any further interference. The prognosis appears to be pathetically hopeless.

Comment

Previous to the revision of the antecedent operation the most frequent and the most troublesome complaints were a sick nauseating feeling, anorexia, bilious vomiting, pale, diarrheal and frothy stools. There was the usual intolerance to a number of foods, particularly milk and concentrated sugars with early and late postprandial symptoms. Seven patients became addicted to opiates. Some were alarmingly emaciated, haggard and depressed with the melancholy appearance reminiscent of victims of Hitler's concentration camps. Many were unable to either attend to their housework or maintain their previous occupations. Four had repeated hemorrhages with no demonstrable jejunal ulcers to account for the bleeding.

Every patient with severe disturbances was subjected to a pantaloon anastomosis. There was no selection on any such diagnostic criteria as reflux or dumping. It is apparent that results cannot be presented on a percentage basis of either success or failure. The composite picture of the multitude of problems, the evaluation of the corrective operations and reflection on intangibles can only be arrived at by a searching review and interpretation of each case history. Nevertheless, it is possible to round up some impressions on the results.

Twenty-two patients obtained significant or substantial benefits. They were able to return to their previous occupation. They were relieved of nausea, bilious vomiting and diarrhea. A good many enjoyed foods which they were not able to tolerate previously. Such postprandial symptoms as sweating, palpitation, lassitude, which used to compel these patients to lie down, disappeared either completely or were mitigated. One lost seven pounds; all others gained from 6 to 50 pounds. There were a number of substantial gains in weight such as 20, 20, 22, 26, 34, 34, 36 and 43. Two patients in this group were only cured of reflux after

the pantaloon anastomosis was dismantled and a Roux type procedure performed. In six patients interpretation of results are debatable. Further surgery to enlarge the jejunal pouch and straighten out a kink is planned in one patient with residual symptoms of reflux (Case 15).

Another patient was cured of reflux but still complains of nausea and considerable abdominal distress. Speculation arises whether there is still some stasis in the afferent loop without vomiting (Case 23).

A housewife, ex-nurse, 47-years old, was subjected to a conventional gastrectomy and vagotomy. She was bedridden for one year and lost 48 pounds in weight. She looked emaciated, haggard and complained of severe symptoms characteristic of the whole gamut of postgastrectomy syndromes. She was addicted to opiates and tried suicide. After the pantaloon anastomosis she was considerably improved. She was able to resume her housework. She consumed large quantities of food without any discomfort and gained 27 pounds in weight. She has only an estimated 3 to 4 feet of jejunum left. Her chief complaint at the present time is bowel distress and a "peculiar feeling in the head" which is constant. Roentgenograms show a definite kink proximal to the anastomosis of the jejunum to the cecum. Since the patient was also subjected to a vagotomy her bowel distress is difficult to evaluate at the present time. Surgery for relief of obstruction is contemplated if the x-ray evidence of mechanical obstruction still persists (Case 12).

In two patients the results were unmistakably disappointing. One woman, who had had a number of antecedent operations, ceased vomiting copious amounts of bile. Nevertheless, she vomits food and occasionally a little bile and has host of other complaints (Case 24). Another woman, with a typical dumping syndrome, became progressively worse (Case 22).

The pantaloon anastomosis was employed in 194 patients with a duodenal ulcer. An uncertain number of these patients have an intolerance to milk and concentrated carbohydrates and are unable to tolerate large meals. I have a personal knowledge of only one patient who is unmistakably disabled because of severe postgastrectomy symptoms. The relation of the pantaloon anastomosis to the incidence of jejunal ulcers need further observation. One patient is known to have been subjected to another operation elsewhere because of a jejunal ulcer, and one is known to have been under medical mangament for a jejunal ulcer. I only had the opportunity to explore one patient after a pantaloon anastomosis for a gastric hemorrhage. There was a small area at the distal angle of the gastrojejunal anastomosis which, on rubbing, bled rather profusely. A competent pathologist failed to diagnose an ulcer in this area. The real appraisal of the pantaloon anastomosis for duodenal ulcer on the basis of comparison with the conventional method must await a longer period of observation. A total of 542 patients with a Hofmeister-Finsterer retrocolic anastomosis for benign lesions have been observed at various periods of time since 1924. The results can unmistakably be considered as very satisfactory.

Summary and Conclusions

Manifestations of a postgastrectomy and postanastomotic side-effect fit into a design of syndromes.

1. Reflux syndrome
2. Dumping syndrome (efferent loop syndrome)
3. Gastric pouch syndrome

Most frequent and serious disabilities resulted from the various mechanisms of reflux.

The interpretation of all the postgastrectomy side-effects on the basis of dumping leads to confusion. The frequency and the role of dumping in the postgastrectomy aftermath need re-assessment.

Thirty patients with crippling postgastrectomy disabilities were subjected to repairative surgery.

Twenty-two patients obtained significant or satisfactory cures.

The postoperative status in six patients is debatable. Technical errors, still amenable to corrective surgery, are accountable for some of the unsatisfactory results.

The results in two patients were unmistakably disappointing.

The Hofmeister-Finsterer retrocolic anastomosis for nonmalignant lesions was employed in 542 consecutive gastrectomies with a mortality of 1.66 per cent.

The mortality in 280 gastrectomies for benign lesions by the pantaloon anastomosis was 0.71 per cent.

The last gastroenterostmy I performed was in 1925.

The Hofmeister-Finsterer retrocolic anastomosis gives good functional results if the resection is not too extensive.

The pantaloon anastomosis is more complicated and more time-consuming than the conventional method.

Clear alternatives have not been established between the pantaloon method and the Hofmeister-Finsterer retrocolic method of anastomosis for the treatment of duodenal ulcers.

When an incredibly extensive resection is advocated for duodenal ulcer, the pantaloon anastomosis should have a marked advantage over the Hofmeister-Finsterer retrocolic anastomosis.

There are intangible factors in both methods which are difficult to evaluate.

The pantaloon anastomosis has proved highly beneficial in patients with severe postgastrectomy and postanastomotic side-effects. The pantaloon anastomosis is recommended for malignant lesions with either partial or total removal of the stomach and for highly-situated gastric ulcers.

Twenty-five patients were subjected to partial gastrectomy and 10 to total gastrectomy for malignant lesions by the pantaloon method of anastomosis with a mortality of 4.7 per cent.

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GASTROINTESTINAL COMPLICATIONS OF ANTIBIOTIC THERAPY*

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I have been asked by your president to speak briefly upon the gastrointestinal complications of antibiotic therapy. I shall begin now by making the same confession that I made to the Chairman of your Program Committee several months ago – that I have done no research in this field other than the ordinary clinical observations that we all make in our daily contact with patients. In these three months since I spoke to the Chairman of the Program Committee I have still not done any research on antibiotics, except inadvertently to have become nauseated by aureomycin. I did not pursue the experiment further and as a result I have not even developed diarrhea for the sake of this presentation.

In perusing the literature on this subject I have found out two things. First, that the literature is voluminous, and second, that others have had substantially the same experiences with antibiotics that we have all had, but that hardly any two writers on this subject agree with each other as to the pathogenesis of a particular toxic effect or, surprisingly even as to its treatment. Only for the purpose of organizational grammar have I divided the gastrointestinal complications of antibiotic therapy into five groups.

Allergic Reactions

The first, allergic reactions, we may dismiss, I think, by saying that it is not surprising that the common and uncommon antibiotics, like all other drugs known to the medical profession or to the druggist, are capable of producing a variety of allergic manifestations, chiefly dermatological and sometimes hematological[1,2]. While there have been, to my knowledge thus far, no convincing reports of allergic reactions in the gastrointestinal tract central to the mucous membranes, it seems reasonable to expect hives, at least, to occur in the gastrointestinal tract, just as they do, for example, in Henoch's purpura. So far, however, this is only a speculation, and I mention it only because it is an opportunity for someone to get into the literature with the first case report. I might add that this is one of the few crevices left in this mighty wall of clinical publications.

Toxic Effects on Mucous Membranes

Among a second group of toxic effects observed with the antibiotics are the lesions of the mucous membranes[3]. These have been well described by several different authors and have probably been seen by everyone here today.

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These lesions usually appear after a protracted treatment or high dosage with aureomycin, terramycin, chloromycetin or one of the other newer agents capable of ridding the bowel of its usual flora. There is no easy correlation, however, between the length of treatment and the appearance of the lesions, and there seems to be tremendous individual variability in the susceptibility of the patients to this complication. The lesions usually consist of erythematous areas, the shades varying from light pink to dark red, with or without raw areas, and sometimes whitish plaques. These may appear in the mouth, around the anus, and in the vagina, and they may be accompanied or preceded by burning, paresthesias of various kinds, pain, or in the case of the anus, itching. On the tongue, in addition, the "black tongue" that has previously been observed with prolonged penicillin therapy may sometimes appear[4]. Of particular interest to the gastroenterologist is the fact that these or similar lesions may sometimes appear in the esophagus, and dysphagia of the type seen in the Plummer-Vinson syndrome may occur[5]. Usually the lesions disappear fairly promptly upon discontinuing all antibiotic therapy, but short of cessation of antibiotics I know of no effective treatment other than symptomatic measures. Liver injections have been advocated, but have not proved to be beneficial.

Why do these lesions occur? Many investigators have blamed them upon the now well-documented observation that the prolonged administration of broad-spectrum antibiotics frequently leads to a depression of the natural antagonists of fungi and consequently an overgrowth, usually, of monilia or candida albicans[4,6,7,8]. Certainly these and similar organisms have been found microscopically and culturally in the mucous membrane lesions described above. The coexistence of the lesions and the monilia, however, by no means proves a causal relationship. Whether or not the fungi have anything to do with these lesions is not certainly settled. And if the fungi are in some way involved, it is by no means certain whether they themselves produce the lesions, whether their growth is encouraged by the lesions, or whether the metabolism of these fungi in some way causes the lesions to appear. It has been shown, for example, that many of the normal bacteria in the bowel produce vitamins, particularly in the B group and Vitamin K, which are important in the body's metabolism[9]. It has also been shown that certain of the fungi, including some monilia, do just the opposite; that is, they metabolize some of these vitamins themselves[10]. It is of utmost importance that all of these clues be followed because it is possible, although by no means proved at the present time, that these mucous membrane lesions actually represent deficiency in some essential food substances and that the administration of these substances might enable one to use antibiotics more effectively. There may be an important opening in this problem suggested by the important observation of Dr. William Hewitt, that neomycin, although highly effective in "sterilizing" the bowel as far as the usual bacterial flora are concerned, does not appear to produce these lesions of the mucous membrane, nor their associated complications, even after protracted treatment[11].

Nausea

Perhaps the most common and most frustrating complication of antibiotic therapy is the production of anorexia, nausea, or vomiting. This is particularly distressing since patients who are sickest and most in need of antibiotic treatment are frequently most liable to disturbances in appetite, and also, because the parenteral administration of the very antibiotics which are most apt to cause nausea, such as aureomycin and terramycin, is not easy. This may be no coincidence. Substances in general which are irritating and painful upon intramuscular injection and which upon intravenous administration are prone to cause thrombophlebitis are frequently the same substances which cause nausea when given orally. In other words, the muscles and the veins seem to be susceptible in many cases to the same source of irritation as is the gastrointestinal mucosa. Many remedies have been suggested for preventing nausea, and some of them, such as the administration of aluminum hydroxide gels, seem to be at least partially successful because they reduce the absorption of the drug[12]. Other antacids such as magnesium trisilicate, do not impair absorption[12]. About the only consistently helpful method of treatment that I know of that does not seem to impair the intestinal absorption is to give the drug only immediately following the ingestion of some food, or milk. On several occasions I have seen this simple expedient become the difference between the patient's being totally unable to take the medication and the satisfactory administration of a reasonable dose. It is also, in this regard, of great interest that some recent investigations seem to indicate that in the case of aureomycin and terramycin, one does not very greatly raise blood levels by increasing the dosage from the reasonable levels compatible with a good appetite to the high levels many people have tried in combating severe infections[13]. In desperate infections one should probably still try to give the highest tolerated dose, but too often one sees a minor infection cause a major gastrointestinal disturbance through the medium of aureomycin. Up to 1 or 2 grams of aureomycin daily substantially increases the blood level as compared with lesser doses, but 4 grams usually does not greatly raise the blood level achieved with 2 grams. It is well to remember, however, that in the treatment of amebiasis it may be important to achieve a fairly high dosage in the bowel itself, and thus a dose of 2 or 3 grams daily appears preferable to smaller doses despite a relatively minor difference in blood level of the drug[14].

On rare occasions antibiotics may produce severe gastralgia, including nausea, vomiting, retching and serious hematemesis. I remember treating a physician for shock following copious hematemesis and melena which began on the fourth day of treatment of his sinusitis with aureomycin. It is possible that some of the bleeding may have been due to trauma which was a consequence of the vomiting itself, as in the so-called Mallory-Weiss syndrome, but that this was not the sole factor in the production of the hematemesis was suggested by the physician's observation that the vomitus was bloody when he first began to

vomit and before retching could have played a significant role. It was true, however, that the passage of fairly large amounts of bright red blood by rectum did not begin until the patient had been retching for several hours. Never before or since did the patient experience significant difficulty with his digestive tract.

Diarrhea

As is the case with many other drugs which produce anorexia by direct irritation of the gastric mucosa, aureomycin, terramycin, carbomycin and other similar antibiotics will in many cases produce diarrhea[7]. Like nausea, the diarrhea seems to be influenced greatly by the dosage, by the length of administraion and also by the variable susceptibiliy of different individuals to this toxic effect. The treatment, if it is impossible to stop the drug or reduce the dosage, is symptomatic. There is, however, much less often, a rather persistent form of diarrhea which may follow prolonged antibiotic therapy which does not always subside when the drug is discontinued[15]. This form of diarrhea has been described in the literature and has been attributed to the fungi or antibiotic resistant staphylococci whose growth in the oropharynx, intestine and pulmonary tree are favored by the administration of antibiotics for long periods. Other investigators, however, have suggested that the fungi are merely coincidental, or perhaps even encouraged by the diarrhea itself, as is known to occur in some other conditions. This school of thought holds that diarrhea of this type is a form of sprue or sprue-like state, possibly caused by some deficiency in nutritive requirements. In my opinion, this very interesting possibility should be further investigated, but the present evidence is not conclusive. While excessive amounts of fat are said to have been found in the stool by staining with Sudan 3, and by the microscopic identification of fatty acid crystals, quantitative studies of the stool fat and stool nitrogen have not been done, and certainly one must be skeptical of an alleged response to therapy with liver extract, since an early enthusiasm for this method of treating sprue has not proved to be certainly effective apart from a hematological complication of this syndrome.

Effects Upon the Liver

Finally we come to what is perhaps the most controversial side-effect of common antibiotic therapy, namely the effects of such drugs as aureomycin, terramycin and chloromycetin upon the liver. Here we find a welter of seemingly contradictory evidence. It has been demonstrated, for example, by Gyorgi, Stokes, and Goldblatt, that almost any antibiotic which is effective in sterilizing the bowel will also prolong the life of rats placed upon a diet known to induce necrosis of the liver[16]. The animals will eventually die of hepatic necrosis, but the end is definitely postponed. And yet, we have the observations of Dowling that high doses of aureomycin over a long period of time may produce fatty metamorphosis of the liver[17]. Fraser and his coworkers have shown that the necrosis of the liver which regularly follows ligation of its principal afferent

blood vessels may be prevented by the administration of antibiotics[18], and some clinicians have suggested on the basis of incomplete experimental data that antibiotic therapy may have a place in the treatment of hepatic coma or impending coma. On the other hand it has been claimed by other investigators that intravenous aureomycin will of itself produce abnormalities in certain liver function tests[19]. How are we to reconcile these divergent observations? I think it is impossible to do so with the information that we have available at the present time, and it would appear that we will be unable to form a rational conclusion without knowing the effect of different bacterial flora upon the liver in health and in disease. In the meantime there seems to be no good evidence that antibiotics should not be used whether liver disease be present or not, if there is a definite indication for the antibiotic therapy. In fact, even those who have found some evidence for experimental liver damage by aureomycin do not believe that this work should prevent experimental and cautious use of antibiotics in liver disease where such forms of therapy seem rational.

Summary

In summary, the five principal gastrointestinal complications of antibiotic therapy seem to be: 1) Allergic effects which are not peculiar to the antibiotics; 2) lesions of the mucous membranes, including the mouth, perianal region, and vagina and accompanied by an overgrowth of fungi; 3) nausea, and sometimes vomiting or even hematemesis; 4) diarrhea, and 5) possibly deleterious effects upon the liver, which may be overshadowed by other effects of the antibiotics which may be beneficial to the liver.

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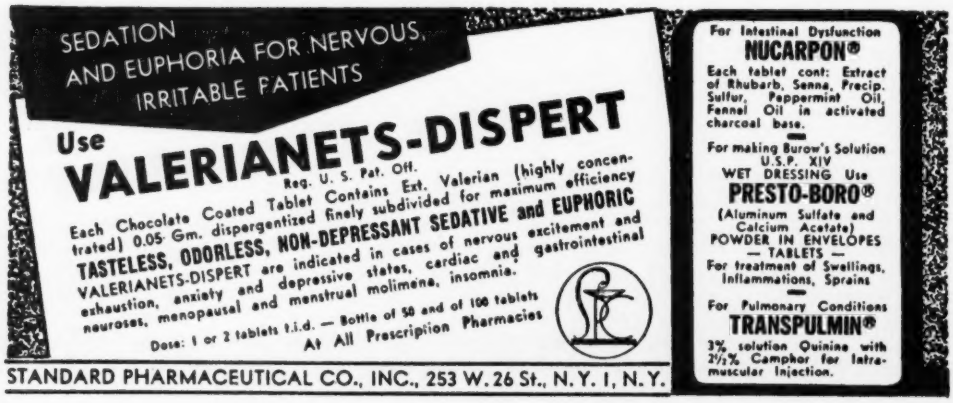

MAGNESIUM ALUMINUM HYDROXIDE GEL IN THE ANTACID THERAPY OF PEPTIC ULCER

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A series of 136 cases in which magnesium aluminum hydroxide gel† was used as an antacid for palliative relief of peptic ulcer and hyperchlorhydria provides an opportunity to evaluate this drug in comparison with aluminum hydroxide gel alone. In my experience, magnesium aluminum hydroxide gel proved more satisfactory in therapeutic efficacy and also had certain other advantages; namely, better palatability and freedom from constipating effects, dryness and astringency.

Literature

It is generaly recognized that medical treatment has a definite place in the management of peptic ulcer. Thus Palmer[1] writes: "The therapy of peptic ulcer is essentially medical; surgery, if indicated, is usually undertaken for the complications of ulcer, less frequently for the lesion itself."

Medical statistics support this belief. Smith, Boles and Jordan[2] of the Lahey Clinic in 1953, in a series of 1,000 cases of gastric ulcer, reported a ten-year follow-up study of 99 patients who had been treated without surgery. They said: "It seems reasonable, therefore, to conclude that a month or less of intensive medical management in many cases of gastric ulcer is justified."

In a follow-up of 687 roentgenologically diagnosed cases of gastric and duodenal ulcer, Malmros and Hiertonn[3] in 1949 reported that the first results of medical treatment were favorable in that 93.5 per cent of cases no longer showed a crater on roentgenological examination. The follow-up study, however, in this series was not so favorable as to permanent results.

Gastric antacids "are employed by physicians chiefly in the treatment of hyperchlorhydria and peptic ulcer" (Goodman and Gilman[4]). There pharmacologists point out the dangers of alkalosis and acid rebound from sodium bicarbonate and the advantages of the nonsystemic, adsorbent antacids. The most important of the latter antacids are aluminum hydroxide gel and magnesium aluminum hydroxide gel (Maalox).

The *United States Dispensatory*[5] reports: "The most important medicinal use of aluminum hydroxide is in the treatment of peptic ulcer in which the per-

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†The magnesium aluminum hydroxide gel used in this clinical study was Maalox Suspension and Tablets. It was supplied for research through the courtesy of William H. Rorer, Inc., of Philadelphia.

TABLE I

ANALYSIS OF 136 CASES TREATED WITH MAALOX

Case	Sex	Age	Duration (months)	Diagnosis	Associated Medication	Constipation	Dryness
1	F	49	7	Hyperacidity	Proloid	0	0
2	F	63	7	Gastric ulcer	None	0	0
3	F	51	7	Peptic ulcer	Sedatives	0	0
4	M	51	7	Heartburn	Sedatives	0	0
5	M	52	6	Peptic ulcer	Sedatives	0	0
6	M	57	6	Peptic ulcer	Butisol	0	0
7	M	41	6	Peptic ulcer	Sedatives	0	0
8	M	52	6	Peptic ulcer	Sedatives	0	0
9	F	36	6	Hyperacidity	Sedatives	0	0
10	M	48	1	Peptic ulcer	Sedatives	0	0
11	F	49	6	Hyperacidity	Estrogen	0	0
12	F	39	6	Hyperacidity	Sedatives	0	0
13	F	41	1	Hyperacidity	Sebella	Yes	0
14	F	26	4	Duodenal ulcer	Sebella	0	0
15	M	53	3	Duodenal ulcer	None	0	0
16	F	66	3	Hyperacidity	Sedatives	0	0
17	F	36	6	Hyperacidity	Butisol	0	0
18	M	63		Peptic ulcer	None	0	0
19	F	22	6	Duodenal ulcer	Sebella	0	0
20	M	50		Duodenal ulcer	Phenobarbital	0	0
21	F	43	1	Hyperacidity	Donnatal	0	0
22	F	26	1	Hyperacidity	Bentyl with phenobarbital	0	0
23	M	51	5	Hyperacidity	Vitamins	0	0
24	F	54	7	Duodenal ulcer	Sedatives	0	0
25	M	45	6	Hyperacidity	Butisol	0	0
26	F	32	7	Peptic ulcer	Banthine and sedatives	0	0
27	F	53	6	Postoperative ulcer	Paredrine-S	0	Yes
28	F	68	6	Gastric ulcer	Sedatives	0	0
29	M	55	6	Peptic ulcer	Donnatal	0	0
30	F	36	2	Hyperacidity	Sebella	Yes	0
31	F	42	6	Hyperacidity	None	0	0
32	M	34	2	Heartburn	None	0	0
33	F	67	1	Heartburn	None	0	0
34	M	53	3	Peptic ulcer	None	0	0
35	F	58	1	Heartburn	Nitranitol	0	0

ANALYSIS OF 136 CASES TREATED WITH MAALOX (*continued*)

Case	Sex	Age	Duration (months)	Diagnosis	Associated Medication	Constipation	Dryness
36	M		4	Heartburn	Syntil	0	0
37	M	68	2	Hyperacidity	Sebella	0	0
38	M	53	2	Pyloric ulcer	Sedatives	0	0
39	F	31	1	Hyperacidity	None	0	0
40	F	39	1	Peptic ulcer	None	0	0
41	F	22	1	Hyperacidity	Bentyl with phenobarbital	0	0
42	F	57	5	Peptic ulcer	None	0	0
43	M	51	1	Spastic	Nembutal and Belladonna	0	0
44	M	43	2	Hyperacidity	None	0	0
45	M	55	2	Peptic ulcer	None	Yes	0
46	M	57	2	Peptic ulcer	Sebella	0	0
47	F	39	5	Hyperacidity	Sebella	0	0
48	M	38	7	Hyperacidity	Sebella	0	0
49	M	50	5	Gastritis	Banthine	0	0
50	F	52	5	Hyperacidity	Barbidonna	0	0
51	M	25	2	Hyperacidity	None	0	0
52	M	24	6	Hyperacidity	Butisol	0	0
53	M	57	5	Peptic ulcer	Tr. Belladonna	0	0
54	F	50	5	Hyperacidity	Sedatives	0	0
55	M	54	1	Hyperacidity	Sedatives	0	0
56	M	45	1	Peptic ulcer	Banthine	0	0
57	M	40	4	Peptic ulcer	Sebella	0	0
58	F	54	5	Hyperacidity	Belladonna	0	0
59	M	46	6	Spastic	Bentyl	0	0
60	M	54	5	Hyperacidity	Sedatives	0	0
61	M	39	5	Duodenal ulcer	Vitamins	0	0
62	M	65	1	Spastic	Sebella	Yes	0
63	M	59	5	Spastic	Donnatal	0	0
64	F	43	6	Hyperacidity	Belladonna	0	0
65	F	28	2	Hyperacidity	Fergon	0	0
66	F	36	2	Hyperacidity	Bentyl	0	0
67	F	30	4	Hyperacidity	Bentyl	0	0
68	M	43	1	Duodenal ulcer	Banthine	0	0
69	F	57	4	Hyperacidity	Sebella	0	0
70	M	54	2	Hyperacidity	Sebella	0	0
71	M	48	6	Peptic ulcer	Syntil	0	0
72	M	34	4	Duodenal ulcer	None	0	0

ANALYSIS OF 136 CASES TREATED WITH MAALOX (*continued*)

Case	Sex	Age	Duration (months)	Diagnosis	Associated Medication	Constipation	Dryness
73	F	24	2	Hyperacidity	Bentyl with Phenobarbital	0	0
74	M	46	1	Hyperacidity	Belladonna	0	0
75	M	50	4	Bleeding ulcer	Belladonna	0	0
76	M	64	2	Hyperacidity	Bentyl	0	0
77	F	60	1	Hyperacidity	Veratrum Viride	0	0
78	M	60	4	Hyperacidity	Sedatives	0	0
79	F	64	5	Hyperacidity	Sedatives	0	0
80	F	62	6	Hyperacidity	Donnatal	0	0
81	F	55	4	Hyperacidity	Sebella	0	0
82	F	48	2	Spastic	Bentyl	0	0
83	M	55	2	Spastic	Belladonna	0	Yes
84	M	59	5	Duodenal ulcer	Sebella	0	0
85	M	50	1	Duodenal ulcer	Banthine	0	0
86	F	79	6	Hyperacidity	Bentyl	0	0
87	M	35	2	Duodenal ulcer	Sedatives	0	0
88	M	59	3	Hyperacidity	Banthine	0	0
89	F	69	4	Gastric ulcer	Belladonna	0	Yes
90	M	33	6	Hyperacidity	Banthine	0	0
91	M	40	1	Pyloric ulcer	Belladonna	0	0
92	F	45	2	Spastic	Bentyl	0	0
93	M	17	4	Hyperacidity	Sedatives	0	0
94	M	55	4	Duodenal ulcer	Bromural	0	0
95	F	50	4	Spastic	Banthine	0	0
96	M	58	4	Spastic	Sedatives	0	0
97	M	57	2	Hyperacidity	Sebella	0	0
98	M	39	4	Duodenal ulcer	Sedatives	0	0
99	M	60	5	Spastic	Sedatives	0	0
100	M	36	4	Hyperacidity	Bentyl	0	0
101	F	33	3	Duodenal ulcer	Sebella	0	0
102	M	67	4	Duodenal ulcer	Phenobarbital and Belladonna	0	0
103	M	47	4	Pyloric ulcer	Sebella	0	0
104	M	37	2	Spastic	Sebella	0	0
105	M	48	5	Duodenal ulcer	Banthine	0	0
106	F	52	2	Spastic	Sedatives	0	0
107	F	53	5	Gastric ulcer	Vitamins	0	0
108	M	45	2	Spastic	Bentyl	0	0

ANALYSIS OF 136 CASES TREATED WITH MAALOX (*concluded*)

Case	Sex	Age	Duration (months)	Diagnosis	Associated Medication	Constipation	Dryness
109	M	63	2	Spastic	Bentyl	0	0
110	M	62	4	Duodenal ulcer	Donnatal	Yes	0
111	M	37	2	Hyperacidity	Bentyl	0	0
112	M	40	4	Duodenal ulcer	Sedatives	Yes	0
113	M	44	1	Spastic	None	0	0
114	M	28	2	Hyperacidity	Bromural	0	0
115	M	69	4	Spastic	Belladonna	0	0
116	F	42	2	Hyperacidity	Bentyl	0	0
117	F	33	4	Spastic	Sedatives	0	0
118	M	45	4	Hyperacidity	Sebella	0	0
119	M	50	3	Duodenal ulcer	Banthine	0	Yes
120	M	56	3	Hyperacidity	Bentyl	0	0
121	M	55	3	Duodenal ulcer	Sebella	0	0
122	M	28	4	Spastic	Barbidonna	0	0
123	F	75	3	Spastic	Belladonna	0	0
124	M	26	2	Duodenal ulcer	Phenobarbital	0	0
125	M	29	3	Spastic GI	Banthine	0	Yes
126	F	26	3	Spastic GI	Sebella	0	0
127	F	51	3	Spastic	Sedatives	Yes	0
128	F	41	3	Hyperacidity	Barbidonna	0	0
129	F	72	3	Spastic	Belladonna	0	0
130	M	46	2	Spastic	Sedatives	0	0
131	M	27	2	Spastic	Donnatal	Yes	0
132	M	40	2	Duodenal ulcer	Sedatives	0	0
133	F	58	3	Spastic	Banthine	0	Yes
134	F	63	2	Spastic	Donnatal	0	0
135	M	39	2	Duodenal ulcer	Bromides	0	0
136	F	26	2	Spastic	Bentyl	0	0

sistence of its antacid effect is of especial importance, but it appears also to act as a protective in these cases and to exercise some other beneficial, perhaps astringent, action beyond that of merely correcting the acidity; it is probable that it has a protective action on the raw surface."

At the Cleveland Clinic, Collins[6] in 1945 reported favorably that aluminum hydroxide gel had been included in the treatment of more than 3,000 patients in a period of eight years, and that it was "the principal substitute for absorbable alkalis in the antacid therapy of peptic ulcer".

Aluminum hydroxide gel, however, has three disadvantages: (1) unpleasant taste, (2) astringency causing dryness of the mouth and throat from absorption of water, and (3) constipating effect. The third disadvantage is the most serious.

With reference to aluminum hydroxide gel *New and Non-Official Remedies*[7] (1953) states that "because of its astringency, it may cause constipation". The *United States Dispensatory*[5] says: "Its constipating action is its chief disadvantage".

Impactions and intestinal obstruction have been reported from aluminum hydroxide gel, writes Bastedo[8]. "*Disadvantages* are that it lessens the absorption of phosphates and iron, that it irritates the stomach and is nauseating to a number of patients, that it is constipating, and that it is slow in action".

Kraemer[9] in 1938 described frequent constipation and the occurrence of fecal impaction in 2 cases from the use of collodial aluminum hydroxide. Havens[10] in 1939 reported a death from intestinal obstruction caused by colloidal aluminum hydroxide used in the treatment of bleeding duodenal ulcer.

In his report of antacid therapy for peptic ulcer, Collins[6] observed the constipating effect of aluminum hydroxide gel and suggested: "If constipation is unusually troublesome, combinations of aluminum hydroxide gel and magnesium trisilicate are used".

Magnesium Aluminum Hydroxide Gel

The combination of magnesium hydroxide with aluminum hydroxide gel (Maalox) is equally effective in the antacid therapy of peptic ulcer and at the same time avoids the astringency and constipating effect of aluminum hydroxide gel administered alone. Magnesium hydroxide and oxide are nonalkalizing antacids of prolonged action which also overcome the undesirable side-effects of aluminum hydroxide gel. The *United States Dispensatory*[5] reports: "Magnesium oxide is used in medicine chiefly as a gastric antacid. One gram will neutralize approximately 500 c.c. of 0.1/N hydrochloric acid. The compound is insoluble and solution, following ingestion, is not effected until the drug reacts with the gastric hydrochloric acid to form magnesium chloride. Because of this interaction, the neutralizing action is slower than that of sodium bicarbonate and more prolonged. Also, it has the advantage that that portion which is not used in the immediate neutralizing action at the time of administration tends to remain in the stomach and thus serves to neutralize acid which is subsequently secreted".

In a comparative study of 12 groups of antacids, including a total of 37 drugs, Steigmann, Hardt and Hyman[11] in 1952 found that magnesium hydroxide in combination had the greatest and longest action. Lawrence[12] in 1952, in a study covering 140 medically treated cases of peptic ulcer, reported that magnesium antacids produced greater and more rapid relief of pain than aluminum hydroxide.

As far back as 1937 Friedenwald and Morrison, in an article published in the *Journal of the American Medical Association*, pointed out that aluminum hydroxide is a useful antacid which produces no systemic reactions such as

alkalosis or other toxic symptoms; and that magnesium hydroxide is a valuable aid in the treatment of peptic ulcer and hyperacidity[13].

Rossett and Rice state: "Aluminum hydroxide gel combined with milk of magnesia is a much more effective antacid than aluminum hydroxide gel alone"[14].

By use of an *in vitro* method for continuous recording of pH, beginning with a pH of 1.4, and providing for the addition of 240 c.c. 0.1/N hydrochloric acid hourly, these authors demonstrated that 10 c.c. of a colloidal suspension of magnesium and aluminum hydroxides (Maalox) maintains a pH of more than 3 for over an hour, whereas an identical test using 15 c.c. of one brand of aluminum hydroxide maintains a pH of 3 for less than thirty minutes[14].

In my experience Maalox (magnesium aluminum hydroxide gel) is preferable to aluminum hydroxide gel because it is more palatable, better tolerated by the stomach, and does not cause constipation or undue astringency. It may be described as a palatable, antacid, demulcent, nonconstipating, colloidal suspension of magnesium and aluminum hydroxides, useful for the relief of gastric hyperacidity. The average dose as an antacid and protective is 2 to 4 teaspoonfuls, which may be given in water or milk twenty minutes after meals and on retiring. Maalox Tablets contain 0.4 gm. of the combined hydroxides of magnesium and aluminum and are approximately equivalent to a teaspoonful of the liquid suspension. Magnesium aluminum hydroxide gel is contraindicated in cases of severe debility or renal failure.

Maalox is described in Remington's *Practice of Pharmacy*[15] (1951) as follows: "Maalox (Rorer)—Liquid suspension of magnesium and aluminum hydroxides. *Uses:* antacid. *Dose:* 2 to 4 teaspoonfuls with water after meals".

Clinical Report

Magnesium aluminum hydroxide gel was administered as an antacid to 136 adults ranging in age from 17 to 79. Both the liquid suspension and tablets were used. There were 79 males and 57 females. The diagnoses were peptic ulcer 50 cases, hyperacidity 52 cases, heartburn 5 cases, spasticity 28 cases, and gastritis 1 case. The duration of the symptoms ranged from 1 month to 7 months, average 3.5 months.

As shown by the table, constipation was reported in only 8 of the 136 cases (5.9 per cent). It was never so serious as to require discontinuance of the medication.

I observed that those patients who were not suffering from constipation prior to taking magnesium aluminum hydroxide gel did not develop this trouble during the treatment. Only those patients suffering from severe constipation before using Maalox continued to be constipated. In a number of cases of

persons suffering from mild constipation, it was noted that this complaint was somewhat relieved during the therapy.

Dryness of the mouth and throat was observed in only 6 of the 136 cases (4.4 per cent). In 5 of these cases the dryness could definitely be accounted for by the associated medication (Banthine 3, belladonna 2).

Conclusions

1. Magnesium aluminum hydroxide gel is superior to aluminum hydroxide gel in the antacid therapy of peptic ulcer and hyperchlorhydria.

2. Magnesium aluminum hydroxide gel avoids the astringency and constipating effects of aluminum hydroxide gel. In a series of 136 cases, only 8 patients complained of constipation. All of these patients had suffered from severe constipation before beginning treatment with magnesium aluminum hydroxide gel.

3. Magnesium aluminum hydroxide gel avoids the dryness of the mouth and throat often associated with the dehydrating action of aluminum hydroxide gel. This complaint was present in only 6 of the 136 cases, in 5 of which it could be accounted for by the associated medication.

4. Magnesium aluminum hydroxide gel is more palatable than aluminum hydroxide gel and better suited to the prolonged administration required for the antacid therapy of peptic ulcer and hyperchlorhydria.

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RESECTION OF THE LIVER*

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The practicability of resecting a portion of the liver has been proved for many years[1]. Cures for as long as nine years following the removal of malignant tumors involving the liver have dispelled doubt as to the value of the procedure[2]. Despite reports of successful cases, surgeons have always considered the removal of segments of the liver a formidable procedure. They have naturally been concerned as to the amount of liver they could safely remove without seriously disturbing its function and about their ability to control hemorrhage adequately[3].

Fishback and others have shown experimentally that four-fifths of the liver of animals may be safely removed[4,5]. The regenerative capacity of the liver partially destroyed by disease processes and trauma has been demonstrated on numerous occasions[6,7]. The right and left branches of the hepatic artery anastomose freely so that if either main branch is divided during a resection, the intact branch can adequately supply the remaining portions of the liver[8]. The vascularity of the liver, as Duckett and Montgomery have pointed out[3], favors the removal of any part of the liver without jeopardy to the nutrition of the remainder. One must not, however, damage the main hepatic artery[9,10]. Death always follows ligation of the hepatic branch of the hepatic artery at its entrance into the liver, Mann and his co-workers[10] reported, although ligation at the point of origin is without effect. If the hepatic artery is compressed for more than 10 minutes, Shallow and Wagner have stated[11], a profound fall in blood pressure is observed. After radical operation for advanced carcinoma of the hepatic ducts, Brunschwig and Bigelow[12] reported autopsy findings, including liver infarcts, resulting from damage to the hepatic artery.

As managing bleeding is the primary concern in liver surgery, the various methods of hepatic resection merely represent the various ways of controlling hemorrhage.

Early attempts to remove tumors of the liver were made by compression of the tumor stump with elastic ligature with extraperitonealization of the stump (Cousins 1874)[12]. The tumor was cut distal to the ligature or allowed to slough off. Von Eiselberg[13], in 1893, and Von Rosenthal[14], in 1897, reported the use of the cautery and the packing of the raw edge of the liver with gauze to aid hemostasis. Another early method reported by Clementi[15] in 1890, was to apply one or more clamps to the base of the tumor and leave them in place. In 1899, Keen[1], resecting the left lobe of the liver for carcinoma, burned through the pedicle with a cautery, ligated the larger vessels, and closed the open part with

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catgut sutures and a gauze pack. In 1942, Schumaker[16] removed an angioma of the left lobe of the liver. He reviewed 56 resections for angioma of the liver. Pickerell and Clay[17], in 1944, reported three cases of resection of the left lobe of the liver. Otherwise, only single cases have been reported.

Since January, 1946, I have resected a portion of the liver in 16 patients. Table I lists the conditions for which resection was performed.

TABLE I

1. Primary Benign Tumors of the Liver	
a. Hepatoma	2
b. Hemangioma	2
2. Primary Malignant Tumors of the Liver	
a. Hepatoma	0
b. Cholangioma	0
3. Secondary Malignant Tumors of the Liver	5
4. Hepatic Portal Obstruction	
a. Benign	1
b. Malignant	5
Total	15

Primary liver tumors are of four general classes: tumors of the liver cells (hepatomas), tumors of the bile duct cells (cholangiomas), mixtures of these two types, and tumors of the supporting structures. Any of these types may be benign (adenoma) or malignant (carcinoma or sarcoma)[18].

After any injury to hepatic tissue, regeneration is attempted. Because the forces normally limiting regeneration after injury are not well developed in the liver, the regenerative process is often so excessive that it results in adenoma and later even carcinoma. There is a uniform gradation between nodular hyperplasia, multiple adenoma, and multiple carcinoma. These three stages may be seen at one time in one liver[19].

Primary Carcinoma of the Liver

Primary carcinoma of the liver is uncommon although Warvi[20] found 1,200 cases which had been studied up to 1944. Strong and Pitts[21] found an incidence of 7.19 per cent for primary carcinoma of the liver in autopsies on Chinese from a province in South China where a high percentage of the population had liver parasites. This same study of 1,828 autopsies reported only two white patients with primary carcinoma of the liver, an incidence of 0.19 per cent.

When carcinoma involves the liver, either primarily or secondarily, the prognosis for the patient is usually considered hopeless. Brunschwig[22], however, described a case reported by Wendel in which a large carcinoma involving most of the liver was resected along with the adhering gallbladder. Two years later, the patient was again operated on for recurrence of the malignancy in the nodes of the right retroperitoneal space. Resection of the right colon, retroperitoneal

lymphatic, and areolar tissues was carried out. The patient survived seven years. He died nine years after this original operation from carcinomatosis including involvement of the markedly hypertrophied left lobe of the liver.

The only hope for patients with carcinoma of the liver is when the lesion is single and when resection can be carried out[23]. No primary malignant tumor of the liver in my series fell into this category.

Two benign hepatomas which, according to Ewing, frequently become malignant tumors, were encountered and resected. A typical case follows.

A white woman, aged 34, complained of pain in right lower abdominal quadrant and of irregular and profuse menstrual periods. Physical examination revealed a mass in the right adnexal region. At operation a 10 cm. ovarian cyst was found in the right side. A right salpingoophorectomy was performed. During routine exploration of the abdomen after this procedure, a 2 cm. nodule was discovered on the anterior superior surface of the right lobe of the liver. Deep overlapping mattress sutures of chromic catgut were placed through normal liver tissue adjacent to the nodule. Then the firm round mass of tumor was excised. The mattress sutures were tied, and Glisson's capsule was approximated with a running stitch of fine catgut suture material.

The pathological report is as follows: Sections of the liver revealed a poorly demarcated partially encapsulated nodule. It consisted of cords of liver cells of normal appearance. These cells presented irregularly distributed bile ducts which attempted to form the usually associated lobular architecture of the liver. This phase was evident in portions of the nodule. Liver parenchyma surrounding this nodule presented infiltration by slight round cells in periportal areas and slight accentuation of fibroconnective tissue. Fine brown granules were present in liver cells adjacent to central venules.

After convalescing without incident the patient has remained well for five and one-half years.

Tumors of the supporting structures, including blood vessels and fibrous tissue, also occur infrequently. Shallow and Wagner[11] reported a primary fibrosarcoma of the liver weighing 5,200 grams and quoted the reviews of Jaffe[24] Goldstein[25], and Miller[26]. This study suggests that the total number of cases of primary sarcoma of the liver studied histologically is probably still not more than 100.

Wilson and Tyson[27] have reviewed the literature regarding the incidence of hemangioma of the liver. They were able to collect 84 cases of hemangioma of the liver that had been operated on. Resection of the tumor was performed in 71 of these cases. Surgeons do not often encounter large hemangiomas of the liver. They occasionally see small ones, practically always cavernous, during a laparotomy or autopsy. D'Errico[28] has emphasized the seriousness of spontaneous

or accidental rupture of these lesions. He found reports of 14 cases in which rupture occurred, with death in all but two[29].

Mantle[30] reported a death from hemorrhage resulting from aspiration of a hemangioma of the liver with a fine needls during a laparotomy. Biopsy of a hemangioma may present a difficult problem in controlling hemorrhage. It is generally agreed, however, that regardless of size these specimens may be removed surgically if the resection is carried out through normal liver tissue rather than through the vascular tumor. Two hemangiomas of the liver were removed in this series. The following case is typical.

A 58-year old man entered the hospital for the repair of an inguinal hernia. His postoperative course included more than the usual amount of indigestion and distention. Close questioning revealed that the patient had tolerated fatty foods poorly for three years. A roentgen series of the gallbladder indicated that it functioned poorly and contained stones.

At abdominal exploration 10 days after the inguinal hernia repair, a thickened gallbladder with many stones was demonstrable. In addition, a tense, soft, purplish tumor mass measuring 1½ x 1 x 4 cm. was discovered on the inferior surface of the liver medial to the attached gallbladder. The cystic duct and cystic artery were clamped, divided and ligated. The gallbladder was removed from the cystic duct outward. During this procedure, the contiguous vascular tumor was inadvertently ruptured. It collapsed and bled profusely. The hemorrhage could not be controlled with pressure. Deep chromic catgut sutures were placed through the normal tissue around the tumor with a large, dull curved needle. The tumor, together with a 2 cm. cuff of normal liver tissue, was excised. Gelfoam was placed in the defect, and the catgut sutures were tied over the gelfoam. A tube and Penrose drain were placed in the Morrison's pouch and brought out through a stab wound. The abdomen was closed in layers. The patient's convalescence was complicated by a moderate atelectosis. Discharged on the 10th postoperative day, he has remained well.

Secondary Carcinoma of the Liver

The liver is very often the site of metastatic disease. It may occur by direct extension, as in some patients who have carcinoma of the gallbladder, stomach, or transverse colon. It may be involved by direct extension through the lymphatics from carcinoma of the colon or by embolic spread from the invasion of blood vessels frequently associated with these and other tumors[23].

Surgeons should realize that metatastic carcinoma of the liver is deceiving. These tumors often present themselves as one or more, hard, raised, yellow-white nodules which, as they grow larger, degenerate in the center and assume a characteristic umbilicated appearance. Occasionally they are found on the surface of the liver. They may be detected on palpation by their firm consistency deep in the liver substance. It is important to realize that benign

tumors of the liver may have the appearance of metastatic malignant lesions. I performed what I thought to be a palliative resection of a malignant lesion in the colon in 1934. The patient had a visible and palpable nodule in the liver. He has not missed a day's work in 19 years. Brunschwig[22] has emphasized that one often cannot tell by inspection or palpation whether a solitary liver nodule is benign or malignant. He added that the presence of one or several small nodules in the liver when there is a resectable neoplasm within the abdomen should not deter removal of the neoplasm because the nodules are assumed to be metastatic. He stressed that when such nodules are excised and examined histologically, they are not infrequently found to be fibromas, scirrhous angiomas, or small cysts. Biopsy and frozen section should always be done if the operative procedure depends upon whether or not they are metastatic.

Brunschwig[22] also emphasized a second important point: when the liver is involved by direct extension from a carcinoma of the stomach or colon, the actual involvement is often less than it appears.

Wangensteen[30] has suggested that, when a single hepatic metastasis exists, it be excised at a second operative procedure following the resection of the primary growth. On five occasions I have resected the primary tumor and a single hepatic metastasis at a single operation. Three of these lesions appeared to extend to the liver by contiguity and two by extension through the lymphatics. The primary lesion was in the gallbladder in one patient and in the stomach in another. The two cases which appeared via the lymphatics were primary in the colon.

I think that excellent palliation was obtained in the first two instances but none in the second. Following are the case reports.

Case 1:—A 74-year old white man was admitted to the hospital on March 8, 1947. He complained of recurrent attacks of severe epigastric pain, episodes of vomiting bloody material, and the passage of copious, tarry stools.

The patient was undernourished and showed signs of dehydration and recent weight loss. Abdominal examination revealed a fixed, irregular, nontender mass in the midepigastrium. Gastrointestinal roentgenograms demonstrated a large obstructing defect in the prepyloric area of the stomach.

At operation, the abdomen was entered through an upper transverse incision. Exploration of the stomach revealed the presence of a large carcinoma which appeared to involve the distal half of the stomach. The tumor was adherent to, and extended into, the outer portion of the right lobe of the liver. The mass also adhered to the head and the proximal portion of the body of the pancreas. The omentum was removed from the transverse colon, and the lesser peritoneal cavity explored. The tumor mass was separated from the pancreas without difficulty or excessive bleeding. The neoplastic mass involving the stomach was removed from the right lobe of the liver by blunt dissection. The cancer tissue

obviously extended into the liver. The duodenum was divided 2.5 cm. distal to the pylorus, and the stump was inverted with a continuous catgut and interrupted cotton sutures. A high subtotal gastric resection was accomplished, and the Hofmeister modification of the posterior Polya method was used to restore gastrointestinal continuity.

Deep matress sutures of #2 chromic catgut were placed through the outer one-third of the right lobe of the liver, and a portion of the liver tissue well past the border of the neoplasm was excised. The segment removed was cut so that the remaining edge of the liver presented a beveled trough.

Oxycel gauze strips were placed along the cut edge of the liver, and the beveled edges were approximated with chromic catgut. The abdomen was closed in layers without drainage. Blood loss was estimated and replaced during the operation.

Pathology:—The patient had severe (mucoid) ulcerative adenocarcinoma of the stomach with metastasis by direct extension into the surface of the liver.

On the second postoperative day, the patient developed auricular fibrillation and pulmonary edema. Fluids were restricted, and parenteral digitalis was administered. The arrhythmia subsided on the fourth postoperative day. The patient was discharged from the hospital on the 19th postoperative day. He maintained normal weight and nutrition, and he showed no evidence of persistent or recurrent cancer when he died on August 8, 1951.

The end results in the surgical treatment of carcinoma of the stomach can be improved only by early diagnosis and extensive excision of the cancer-bearing portion of the stomach and contiguous organs.

The preceding case was presented to show that adequate resection of the stomach and adjacent organs with cancer-bearing tissue can prolong life and increase the patient's comfort although the primary lesion is large and the liver is invaded. The technic of partial hepatectomy is illustrated.

Case 2:—A 62-year old woman had had infrequent attacks of gallstone colic for 10 years. Three months before hospital admission, the attacks began to recur at weekly intervals. The patient developed anorexia and intolerance to fatty foods. She complained of feeling weak and of losing 30 pounds in this three-month period. Rigidity and tenderness of the upper right quadrant were the only findings elicited on physical examination. Roentgen studies of the biliary and gastrointestinal tracts were negative except for a nonfunctioning gallbladder.

At operation, the gallbladder appeared to be enlarged, firmly thickened, and obviously neoplastic. The ampulla was normal in size and consistency, and the fundus adhered to the under surface of the right lobe of the liver. Tumor tissue invaded the liver at this point. The common bile duct was dilated and thickened. The pancreas was normal to palpation and visualization.

The common bile duct was opened and myriads of small stones aspirated and removed with a scoop. Unattached meaty tissue was scooped from the common bile duct. From frozen section studies, the pahologist concluded that this was tumor tissue. A 5 mm. bougie was passed into the duodenum without difficulty. Both hepatic ducts were explored from within and appeared to be patent. The bile ducts were irrigated. Then a number 14F. "T" tube was placed in the common bile duct, and the opening closed with fine catgut suture to and beyond the "T" tube. A circular portion of the common bile duct around the entrance of the cystic duct was excised, and this wound was closed transversally. The gallbladder was removed from the cystic duct outward. The dissection was carried out without difficulty until the proximal portion of the fundus was reached at which point tumor tissue had broken through the wall of the gallbladder and invaded the liver. Through and through overlapping mattress sutures were placed through healthy liver tissue proximal to the area of tumor invasion, and this portion of the right lobe of the liver was resected in continuity with the neoplastic gallbladder. The mattress sutures were tied, gelfoam placed over the raw liver surface, and Glisson's capsule was approximated with fine gastrointestinal suture material. Two Penrose drains were placed in Morrison's pouch and brought out through a stab wound lateral to the abdominal mission. The "T" tube was brought out through the omentum and a stab wound medial to the incision. A routine closure was performed.

The patient's postoperative course was uneventful. A cholangiogram on the 10th postoperative day showed that the media flowed freely into the doudenum. The patient, discharged on the 14th postoperative day, has remained well for nine months. My experience with carcinoma of the gallbladder suggests that resection of this portion of the liver added to this patient's survival time.

Case 3:—A 70-year old woman with severe cramp-like abdominal pain was admitted to the hospital. Physical examination revealed a distended abdomen with some tenderness and rebound pain over the cecum. A scout roentgenogram taken shortly after admission presented the typical pattern of an obstructed left colon. A decompression procedure was deemed necessary, and a cecostomy was performed eight hours after admission. The patient's postoperative course was uncomplicated. Barium enema studies eight days after the cecostomy disclosed a constricting neoplasm in the splenic flexure of the colon.

At operation three days later, an obstructing carcinoma involving the splenic flexure of the colon was demonstrated. There were no demonstrable glands in the mesentery or along the aorta. When the liver was explored, however, a 4 cm. solitary metastasis was found in the left lobe of the liver. A left hemicolectomy was performed and gastrointestinal continuity established by an end-to-end transverse sigmoidostomy. The mesentery was excised, and the remaining portion approximated. Overlapping mattress sutures of chromic catgut suture were then placed through the entire thickness of the left lobe of the liver just distal to the triangular ligament of the liver. The left lobe of the liver containing

the solitary nodule was excised. A strip of oxycel gauze was placed over the raw edge of the liver and the mattress sutures were tied. Glisson's capsule was approximated with fine gastrointestinal suture. A Penrose drain was placed in the left upper abdominal quadrant, and a routine closure was carried out. The patient convalesced from the operation without incident, however, she died from generalized abdominal metastasis six months after the procedure. It is doubtful if the palliation received in this instance was of sufficient value to warrant an undertaking of such magnitude.

A third category of resection of the liver included resections of the left lobe to find a bile duct in patients having an obliterated hepatic portal with obstruction of the biliary tract. Longmire[31] originally described this operation which consists of upward dissection of the left lobe of the liver until a suitable duct for anastomosis to the jejunum is found. The following case is illustrative.

Case 4:—A 40-year old farmer was admitted to the hospital on February 14, 1950. He complained of pain in the right upper abdominal quadrant, chills, and periodic attacks of jaundice.

History revealed that this man had had a cholecystectomy for what seemed to be typical gallstone colic one year before this admission. He said that he became deeply jaundiced immediately after this procedure and was extremely ill but did not have pain. The jaundice began to subside in the third postoperative week. The patient remained asymptomatic until June, 1949, four months after the cyolecystectomy. Then he again became deeply jaundiced, had fever and "passed voluminous, foamy, gray-colored stools". He had pain in the right upper quadrant and a disabling itching of his skin for about 30 days. After this episode, he had mild, recurrent febrile attacks but remained fairly well for an additional four months. In November, 1949, he again experienced complaints similar to those of June. The jaundice, fever and itching persisted, but the patient was only partially incapacitated. Five days before the present hospital admission, he became acutely ill with severe pain of the upper right quadrant and chills. Antibiotics, sedatives and antispasmodics were not effective.

Upon physical examination, the patient appeared to be acutely ill. His sclerae were clear, but his skin had an icteric tinge. The border of the liver extended 6 cm. below the costal margin and was diffusely tender. The urinary urobilinogen was positive 1 to 5.

Operation was performed on February 17. Pontocaine subarachnoid block and cyclopropane were used for anesthesia.

The abdomen was entered through an upper transverse incision. The right lobe of the liver was markedly enlarged and contained multiple abscesses varying in size from 1 mm. to 8 cm. in diameter. The material from one of the larger masses was aspirated. It appeared to be odorless pus.

The peritoneum on the lateral surface of the duodenum was divided, and the duodenum was rotated medially. It was impossible to find the common bile duct. A string-like fibrous band, however, extended from the second portion of the duodenum up into the hilus of the liver. The liver parenchyma was dissected away from this stricture for a distance of 2 cm. into the hilus of the liver. At this point a dilated bile duct was encountered. A mucosa-to-mucosa cholangioduodenostomy was accomplished over a polyethylene tube.

The right lobe of the liver was mobilized, and a large abscess in the dome of the liver was aspirated. The liver capsule over this inflammatory process was resected so as to "unroof" the abscess completely. It could be demonstrated that this necrotic cavity extended down to within 1 to 2 cm. of the hilus of the liver. Three Penrose drains were placed in the abscess cavity and one Penrose drain into Morrison's pouch. The three drains were brought out through a stab wound above the transverse incision and the single drain through a separate stab wound beneath the incision. The wound was closed.

The patient's postoperative course was uneventful for the first 10 days. There was a moderate amount of seropurulent drainage around the Penrose drains in the dome of the liver. On February 28 the drainage from the stab wound leading to the liver became more profuse and soon assumed the characteristics of duodenal contents. Constant suction was applied, but the drainage increased in amount. The drainage collected from the duodenal fistula was frequently 3,000 c.c. in a 24-hour period. The patient increasingly presented nutritional and fluid balance problems. On March 31, 41 days after the first operation, a second one was performed.

The abdomen was entered by making an elliptical incision around the fistulous tract with the drains *in situ*. The tract was followed down to the right lobe of the liver. The cholangioduodenostomy was intact, but the opening in the duodenum communicated directly with the old abscess cavity in the right lobe of the liver. The polyethylene tube in the opening was removed and the duodenum separated from the bile duct stump. The opening in the duodenum was then closed. The open bile duct was doubly ligated with chromic catgut, and the drains in the liver were removed. The incision was then extended to the left. The left triangular ligament of the liver was divided and the left lobe of the liver delivered into the wound. Mattress sutures of heavy chromic catgut were placed through the substance of the liver proximal to the triangular ligament. The left lobe of the liver was then excised. A large bile duct was encountered near the center of the remaining portion of the lobe. Green bile was aspirated from this structure.

The jejunum was divided 30 cm. from the ligament of Treitz. The proximal end of the distal loop was brought through the transverse mesocolon and anastomosed to the bile duct protruding from the cut surface of the left lobe of the liver over a polyethylene tube. Gastrointestinal continuity was re-established and

the biliary drainage loop defunctionalized by anastomosing the distal end of the proximal jejunal loop to the side of the distal loop 15 cm. from the cholangiojejunostomy anastomosis.

The patient's postoperative course was quite stormy for the first ten days. On the 10th postoperative day, a right subphrenic abscess was drained by excising a portion of the end of the 11th rib. His convalescence after this drainage was uneventful. Since then the patient has been seen periodically, has regained his normal weight and has maintained an excellent nutritional status.

Intrahepatic cholangiojejunostomy is an operative procedure of considerable risk and magnitude. Moreover, as noted in my first four cases mentioned, it may be performed to relieve biliary tract obstruction in patients with very distressing symptoms in the hope of prolonging their lives.

As demonstrated by the report of this last patient, however, an intrahepatic cholangiojejunostomy may be a life-saving procedure and should have a definite, although limited, place in the armamentarium of every general surgeon.

Conclusions

Surgical removal of substantial portion of the liver is not only indicated but is practical in selected cases. Primary benign tumors of the liver are comparatively easy to remove. If the tumor is malignant with extension to the liver by contiguity, removal of the tumor allows the paient to live longer and more comfortably. In my patients with lymph or blood borne metastases to the liver, removal did not add to the patients' comfort or longevity.

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ISLET CELL TUMORS OF THE PANCREAS

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Although many contributions have been made to our knowledge of islet cell tumors of the pancreas, it is nevertheless important to re-emphasize some of the chief features that occur in this condition. This communication consists of a study of 14 autopsy cases of islet cell adenomata, a review of the literature, and a collection of 32 recently reported cases. Our interest in islet cell tumors was stimulated by experience with the following case, which presented the symptomatology resembling a duodenal ulcer.

Case Report

A middle-aged female complained of intermittent attacks of abdominal distress and epigastric pain. The onset of symptoms were particularly noted during the early morning hours, and these were relieved following breakfast. Her appetite was good and there was often a feeling of hunger sensation. The attacks were accompanied by nervous spells, headaches and vertigo. An x-ray examination of the gastrointestinal tract revealed no abnormalities. The patient continued to have similar attacks with exacerbations and remissions for about four years. Her condition was diagnosed as a duodenal ulcer, for which she was treated, in spite of the repeated negative x-ray findings. She had been re-examined roentgenologically at least four times during this interval and no abnormality was found to account for her symptoms. Finally, her symptoms became increasingly severe and the attacks more frequent which necessitated hospitalization. An x-ray examination during the time in the hospital, likewise, revealed no evidence of ulceration. A routine blood sugar determination revealed a hypoglycemia 50 mg. per cent). At operation an islet cell carcinoma with metastases was found.

Islet cell tumors of the pancreas, while admittedly not too common, probably occur more frequently than is indicated from a perusal of the literature. In 1,319 adult autopsies, we found 14 cases of islet cell adenomas of the pancreas, an incidence of 1 per cent. In a review of 12,000 collected autopsies, it occurred in 0.14 per cent[13]. Others report varying incidences ranging from 0.1 to 0.4 per cent[13,25,4,42,26]. On the other hand, in a careful histologic serial study, 8 islet cell adenomas were found in 500 cases an incidence of 1.6 per cent[33]. There have been several complete reviews of the subject of islet cell adenomas, notably, by Whipple and Frantz[42], who reviewed the literature up to 1944, found 115 published cases; Crain and Thorn[5] collected 258 cases up to 1949, and Howard et al[23]

398 cases up to 1950. In a survey of the more recent literature we found 32 additional cases, 31 of which were functional and 1 nonfunctional.

The etiology of islet cell adenoma is not known. It is believed by some to be of heterotopic origin[22]. Diffuse islet cell hyperplasia has been observed in infants of diabetic mothers, which might have resulted from supplying the mother with insulin during fetal life[41].

In most instances the pancreas appears to be of normal size. It is noteworthy that the pancreas as a rule does not reveal any other abnormalities. In our 14 cases, one pancreas had shown a small cyst, measuring 0.8 cm. in diameter, another revealed an interstitial fibrosis, and in two instances there was a minimal lipomatosis of the pancreas.

Islet cell tumors of the pancreas may be divided into the following groups. (1) Benign islet cell adenoma without hypoglycemia, (2) benign islet cell adenoma with hypoglycemia, (3) benign islet cell adenoma with hyperglycemia, (4) islet cell carcinoma with hypoglycemia, and (5) malignant islet cell adenoma with hyperglycemia. There is also another group of islet cell tumors which histologically appears to be malignant, but clinically seem to be benign. These cases have been designated as questionably or suspicious malignant tumors. Warren[40] gives the following pathologic criteria for the diagnosis of islet cell adenoma: (1) the morphology and arrangement of the cells must resemble those of the islet, (2) there must be a definite capsule, (3) there should be evidence of compression of the adjacent tissue, and (4) the tumor mass must measure at least 1 cm. in diameter.

Benign islet cell adenomas are the most common type. About 90 per cent are benign and 10 per cent malignant. In 39 cases, Whipple[41] found 43 tumors, 27 of which were islet cell adenomas, 3 adenomatosis, 9 questionably malignant tumors and 4 carcinomas. Howard et al[23] collected 398 cases, found 313 or 78.6 per cent were benign.

It is well recognized that not all islet cell tumors are accompanied by functional changes. The functional type most likely originate from the nonfunctional ones. Some adenomas, even though morphologic, closely resemble the structure from which they arise, are not physiologically composed to elaborate the specific hormones. It is difficult to explain why certain islet cell tumors function while others do not. The functioning tumors produce a hypoglycemia, and the nonfunctioning tumors produce no recognizable endocrine manifestations. The functioning type of islet cell adenomata are less common than the nonfunctioning ones. But it must be pointed out, here, that nearly all of the recorded surgical cases were of the functioning type. The incidence of asymptomatic islet cell adenomata is probably greater than hitherto believed. All of our 14 autopsied cases were of the nonfunctioning type.

Calcification in an islet cell tumor may be observed at times. The calcification may be present in visible amounts, which is portrayed in the roentgen examination

or it may occur as a microscopic finding. In our 14 cases, calcification was found in only one instance. In the 32 collected cases it occurred once. Single instances have been recorded by others[19,3,26]. That microscopic evidence of calcification is probably more common is suggested by Lopez-Kruger's[26] finding of calcific changes in 7 of 11 malignant and in 5 of 21 benign adenomas.

Islet cell carcinomata is an uncommon finding in routine autopsy studies. On the other hand its incidence is rather high among surgically recorded cases. In 32 recently collected cases we found nine instances of islet cell carcinoma. According to Lopez-Kruger[26] malignant tumors constitute 18.44 per cent. In the 398 cases of Howard et al[23], there were 37 verified islet cell carcinomas and 48 with suspiciously malignant islet cell tumors.

The criteria for the diagnosis of malignancy is based upon the presence of metastases. Those without metastases are classified as suspiciously malignant. Although, almost all of the malignant islet cell tumors are of the functioning type and produce symptoms of hypoglycemia, there have been a few cases recorded without symptoms[10,15].

Islet cell adenomas are usually round, small in size and encapsulated. They vary from microscopic size to 15 or more centimeters in diameter. The majority measure from 1 to 2 cm. in diameter. In our 14 nonfunctioning cases the average size was 1 centimeter. In 9 of the 31 collected functioning cases, in which the size of the tumor was mentioned, it ranged from 1 to 7 cm., with an average of 2.5 cm. From evidence of collected statistical data, it seems that the functioning islet cell adenomata are somewhat larger than the nonfunctioning ones. It is also of interest to point out that malignant islet cell tumors appear on the average to be larger than benign ones. The average size of the malignant tumors are about 6 cm. in diameter. There have been a few unusually large-sized islet cell tumors recorded in the literature[31,3]. It must be emphasized that the size of the tumor has no relation to its functional activity. A small tumor may give rise to a profound hypoglycemia and vice versa.

The vast majority of islet cell tumors are single. In the clinical cases, approximately from 10 to 15 per cent are multiple. All of our 14 cases of nonfunctioning adenomas were single. The presence of one islet cell tumor does not exclude the existence of a second growth in the pancreas or in an aberrant pancreatic nodule. The occurrence of the number of multiple islet cell tumors vary from two to ten or more. Kalbfleisch[24] reported an instance with five islet cell tumors. In Lopez-Kruger's[26] 44 cases, 35 were single, in 8 there were two tumors and in 1 instance a diffuse islet cell hyperplasia with adenoma was found. In Duff's[10] 233 collected cases, 196 or 87.7 per cent were single, in 20 or 8.96 per cent there were two tumors, in 4 cases there were from two tumors and up to 10 tumors in one of these, and in 3 instances a diffuse adenomatosis was noted.

Islet cell tumors are imbedded in the substance of the pancreas and are not usually palpable. It may be found in any segment, but it is stated to occur

with greater frequency in the tail of the pancreas. In our 14 autopsied cases, it occurred between the head and body in 1, body in 6, tail in 4, and the site not specified in 3 instances. In 27 of 32 collected cases, the tumor was found in the head in 8, in the neck in 1, in between the head and body in 2, in the body in 2, in between the body and tail in 2, in the tail in 8, multiple in 2, and in an aberrant pancreas in 2 cases. Howard et al [23], in 254 of their 398 cases, give the following sites: in the head in 66, in between the head and body in 10, in the body in 62, in between the body and tail in 25, in the tail in 84, and in ectopic in 7 cases.

In our 14 autopsied cases of nonfunctioning islet cell adenomas, there were 5 instances with an associated aberrant pancreas, but the adenomatous growth did not involve any of these. The incidence of islet cell adenoma in an aberrant pancreas is low. In the 32 collected cases, there were 2 with an islet cell tumor involving aberrant pancreatic tissue. One was found adjoining the tail of the pancreas, the other in the retroperitoneal space. In the 398 collected cases of Howard et al[23], there were 9 with an islet cell tumor in an aberrant pancreas[39,43,34,1,38,21,27,37]. The sites of these 9 aberrant pancreatic adenomas were as follows: near the tail, posterior to the head, gastrosplenic, omentum, retroperitoneal, posterior to the tail, between the tail of the pancreas and spleen, near the duodenum, and two in the wall of the duodenum. In addition to the above 9 cases, there are 4 others recorded: 2 in the duodenum[36,12], 1 in the gastric wall[8], and 1 unusual case arising in an aberrant pancreas situated within the liver[1]. In 1 instance in a collected series, there was a malignant adenoma in an aberrant pancreas[5].

The association of diabetes with a functioning islet cell adenoma of the pancreas is very rare. Diabetes, however, is more apt to be found in association with nonfunctioning islet cell tumors. In our 14 autopsied cases of nonfunctioning islet cell tumors, there were 2 instances with diabetes. In Howard et al's[23] 23 cases of nonfunctioning adenomas, 4 were associated with diabetes. In Lopez-Kruger's[26] 44 cases, there were 3 instances of diabetes mellitus.

In a perusal of the literature, there are a few case reports of the association of peptic ulcer with islet cell adenomas. Since the association of peptic ulcer with an islet cell adenoma is a rarity, it must be considered an incidental finding. Although it has been stated that theoretically the association of hyperinsulinism and duodenal ulcer may be expected in view of the experimental and clinical evidence of the effect of hypoglycemia on gastric secretion[6], our clinical experience has not substantiated this observation, in either the functioning or nonfunctioning cases. In our 14 cases of nonfunctioning adenomas, there was only one instance of gastric ulcer and none with duodenal ulcer.

Rarely, a duodenal obstruction may be noted associated with an islet cell adenoma of the pancreas. Such a case has been reported in which a large islet cell tumor in the head of the pancreas compressed the duodenum and caused an obstruction[2].

Islet cell adenomas of the pancreas may be observed at any age, the majority occurring between the fourth and sixth decades. In our 14 autopsied cases, the ages ranged from stillbirth to 87 years. In 258 collected cases, the ages ranged from 6¾ weeks to 68 years, the peak being between 40 and 50 years[5]. It has been pointed out that hypoglycemia symptoms are rarely present in patients over 60 years of age[2]. In 31 collected functioning cases, there were only 2 instances over the age of 60.

The condition rarely occurs in infants and children. In 598 autopsies of infants and children, we encountered one case occurring in a stillborn fetus. The problem arising in this case was whether or not the tumor was of the functioning type and to what extent it affected the fetus *in utero*. Others have reported cases occurring in the newborn[9,17,35]. An interesting case is reported in a child, of an unusually large sized nonfunctioning islet cell tumor which apparently arose in an aberrant pancreas[14]. In 398 collected cases, 14 were found in children below the age of 15 years[23].

The sex distribution is about equal in the functioning cases. In 31 collected cases of islet cell adenomas, 14 were males and 17 females. Approximately, similar incidences have been reported by others[26,5]. In our 14 autopsied nonfunctioning cases, there were 10 males and 4 females.

Functioning islet cell adenoma of the pancreas may be found in all types of patients. It has been pointed out, however, that the patients are nearly always obese[46].

There is often a compelling need for further studies, re-evaluation and emphasis of the symptomatology of islet cell tumors of the pancreas. Because it masquerades the symptomatology of many conditions relating to the digestive and nervous systems, the diagnosis of this condition often challenges the acumen and vigilance of the examiner. Islet cell adenomas may elude discovery for many years, and it is for this important reason that increased awareness of the possibility of the occurrence of this condition should be recognized early. The symptomatology depends in a large measure upon whether the islet cell tumor is functioning or nonfunctioning. It is important to emphasize that in the nonfunctioning adenomas there is no hypoglycemia and therefore no clinical symptomatology.

Islet cell adenoma of the pancreas is a chronic condition, which may run a course of many years and produce a more or less characteristic train of symptoms. The symptoms may vary in severity in the same patient, but are nearly always similar in character. The severity of the symptoms is unrelated to the degree of hyperinsulinism or to the size of the islet cell tumor. Varying intervals of remissions and exacerbations are characteristic. Often the symptoms simulate duodenal ulceration, with the patient awakened in the early morning hours with abdominal distress, relieved by carbohydrate food. At other times the nervous

system symptoms predominate. It should be emphasized here, that the nervous system involvement occurs with greater frequency than with symptoms associated with the digestive tract. Moreover, attention is directed to the fact that not only will fasting bring on the train of symptoms, but also excessive exercise and emotional stress may lead to an attack. The patient early in the course of the disease recognizes that carbohydrate foods immediately relieves the symptoms.

Most of the symptoms encountered in islet cell adenomas are chiefly related to the nervous systems, i.e. nervousness, tremor, profuse sweating, flushing, pallor, vertigo, palpatation of the heart, depression, drowsiness, blurring or double vision, paresthesias, salivation, restlessness, hysteria, weakness, confusion, disorientation, anxiety, clonic and tonic spasms, irritability, positive Babinski, delirium, convulsions and coma. The principal digestive symptoms are abdominal distress, epigastric pain, especially in the early morning hours, which is relieved by food, hunger sensation, nausea and vomiting.

Wilder[44,45] grouped the neurogenic symptoms under the following headings: (1) those related to the central nervous system, (2) those related to the autonomic nervous system, and (3) psychic disturbances. Since it is well known that the effects of hypoglycemia are chiefly on the nervous system, experimental data has shown that the symptoms of hypoglycemia are due to decreased brain metabolism resulting from carbohydrate deficiency. The brain appears to be peculiarly sensitive to hypoglycemia, because its metabolism is entirely dependent on the combustion of glucose and thus the blood sugar assumes a role of special importance in sustaining brain metabolism[26,20]. It has been found that newer areas of brain are the most sensitive and react first to a decreased supply of glucose[20]. The role played by sugar metabolism on the brain is, therefore, particularly significant in the symptomatology of this condition.

The blood sugar determination is singularly the most important, in the diagnosis of clinical cases of islet cell tumors. The dextrose tolerance test has been one of the procedures used in the blood sugar determination, but its usefulness has been abandoned by many in recent years. This has been supplanted by the simple blood sugar test made in the fasting state, in a period of from twelve to forty-eight hours. It may be necessary at times to make repeated tests for the determination of low blood sugars.

Whipple[41] based the diagnosis on the following signs: (1) onset of repeated attacks of nervous, vasomotor and gastrointestinal disturbances in the fasting state, (2) fasting blood sugar of 50 mg. per cent or below per 100 c.c. (hypoglycemia), (3) immediate recovery with the intake of sugar, and (4) electroencephalographic studies showing a reduced alpha rhythm.

In the differential diagnosis it must be borne in mind that there are other factors which influence sugar metabolism. Many organs are involved in the maintenance of a normal blood sugar level. Besides the pancreas, the liver, pituitary,

adrenal, and thyroid glands may play a role in the disturbance of sugar metabolism. Because the brain must be assured of a continuous supply of glucose, this is dependent upon the neuroendocrine balance of carbohydrate metabolism. Lopez-Kruger[26] divided the causes of hypoglycemia into organic and functional. The organic types are due to (a) hyperinsulinism as a result of islet cell adenoma, (b) hepatic disease, (c) pituitary hypofunction (anterior lobe), (d) adrenal hypofunction (cortex) and (e) central nervous system lesions. The functional types are due to autonomonic nervous system imbalance such as occurs in dysinsulinism, renal glycosuria, severe continuous muscular work, pregnancy and lactation, and epilepsy. Extensive hepatic cirrhosis, atrophy or toxicity of the liver are rarely associated with lowering of the blood sugar[7]. Cases of hypoglycemia have been recorded associated with glycogen dysfunction of the liver. Endocrinopathic hypoglycemia other than those of pancreatic origin are not frequent. Depression of blood sugar levels may occur in the crises of Addison's disease and in myxodema.

There are several tests which aid in the differential diagnosis. (1) The insulin tolerance test—after twelve hours of fasting, 5 units of insulin is given intravenously. If an adenoma is present the blood sugar does not reach normal after two hours. (2) Response to adrenalin to rule out any disturbance of glycogen reserve. If the blood sugar does not rise after its administration, it indicates that the hypoglycemic state is due to lack of liver or tissue glycogen, rather than to a primary disturbance in the pancreas[18]. The subcutaneous adrenalin test is also an aid in excluding pituitary or adrenocortical deficiency. Another test to eliminate hypoglyecmia resulting from a deficiency of the hypophysis and adrenals[5] is the administration of 25 mg. of corticotropic hormone. Normally, following this test, there is a lowering of the eosinophils and lymphocytes with a rise in uric acid, but if there is a deficiency of the adrenal and hypophysis, these changes do not occur[16]. To further eliminate a pituitary tumor, roentgenologic examination of the *sella turcica* and examination of the visual fields may yield further information.

Islet cell tumors of the pancreas cannot be diagnosed readily by means of the roentgen examination. Most of the tumors are too small, are imbedded in the pancreatic tissue and do not produce enlargement of the pancreatic organ. The roentgen examination is most useful in eliminating other conditions. In the rare case of a large tumor, it may produce pressure signs on the adjacent organs. In some instances the tumor may show a calcification. Olsson[33] recommended the Engel-Lysholm method for the demonstration of pancreatic tumors. It has been shown that by distending the stomach with an effervescing powder and taking the x-ray in the prone decubitus position, with the rays directed horizontally, the pancreatic bed can be recognized between the spinal column and the stomach[11]. When this space is widened it usually denotes evidence of a pancreatic tumor. Not only may some displacement be observed, but occasionally a pressure filling defect is demonstrated on the posterior wall of the stomach.

Olsson[32] illustrated a case of an islet cell tumor, which produced a smooth localized pressure filling defect on the stomach wall. Macarini and Oliva[28] recommended a combination of pneumoperitoneum and gastric insufflation for the demonstration of pancreatic tumors. They introduced 1,500 to 1,700 ml. of oxygen into the retroperitoneal space, and after 15 minues, the stomach is distended with an effervescing powder. The x-ray is taken in the erect position, and the density of the pancreas is shown between the double air shadows of the stomach and retroperitoneum.

The nonfunctioning islet cell adenomas do not cause symptoms and are not usually recognized clinically. The functioning type, however, sooner or later require surgical removal. Islet cell tumors do not recur after removal, but if there is a postoperative recurrence of hyperinsulinism, it is more apt to be due to multiple adenomas, adenomatosis, malignancy, or an islet cell adenoma located in a remote aberrant pancreas. Benign adenomas, being encapsulated, are readily enucleated. It is not unusual to find that in some cases of hypoglycemia, surgical exploration of the pancreas may fail to reveal evidence of the adenomatous tumor. A number of such instances are recorded in the literature[23,29,30]. Occasionally it is necessary to reoperate and explore the abdomen a second or even a third time, because of the persistence of symptoms, in order to find the islet cell tumor. In one of the recorded cases as many as three operations were performed before the tumor was found. It must be pointed out again that the islet cell tumor may involve an aberrant pancreas, and it may be missed at the original operation. One must also remember that hypoglycemia may be caused by other conditions.

Summary

Autopsy observations of 14 cases of nonfunctioning islet cell adenomas of the pancreas, and 32 recently collected surgical cases are presented in this communication. Islet cell tumors of the pancreas are more common than is usually suspected. The incidence of the nonfunctioning islet cell adenomas is greater than the functioning type. Most islet cell tumors are benign. The problem of malignancy in islet cell adenomas is reviewed. The occurrence of multiple adenomas and adenomas in an aberrant pancreas is described. The size of the tumor in the nonfunctioning cases is usually smaller than in the functioning ones. The condition is not usually associated with other pancreatic abnormalities. Islet cell adenomas are most commonly found in middle age. Its occurrence in the fetus is rare. It was found in a stillborn infant in one of our autopsied cases. The association of diabetes is rare in functioning islet cell adenomas, but it not uncommonly occurs among the nonfunctioning cases. Diabetes occurred in 2 of our 14 autopsied cases. The association of peptic ulcer with islet cell tumors is rare and is an unrelated incidental finding. Functioning islet cell adenomas produce a hypoglycemia which often cause a confusing clinical picture and a diagnostic problem. We have stressed the criteria for the

diagnosis of islet cell adenomas of the pancreas and pointed out its chief clinical features involving the nervous and digestive systems.

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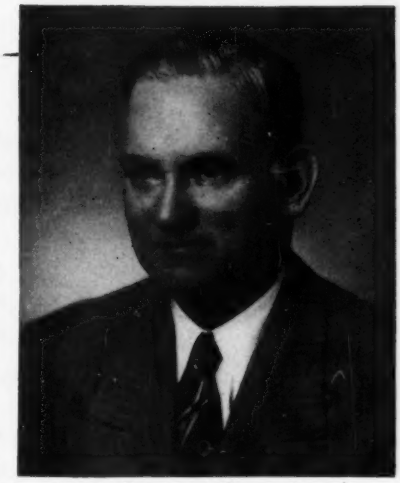

President's Message

The time has come for me to write my last Presidential message. This I find hard to do, because we are just beginning a new era.

This year has been a happy one for me, since there has been change and progress. I hope to see this trend continue, because change can always be in the direction of progress. Moves made which are not progressive may always be altered.

I have been much impressed with the recent articles in Fortune magazine, wherein they designate our economy as a continual state of revolution. There is a great deal to be said in favor of this description of our American economy. Certainly, that characterization is true for medicine. We have seen many radical changes in therapy and many new economic innovations are being tried out. All these facts indicate progress as well as change.

This year has made me indebted to you officers and members of the Council, now the Board of Trustees. Everyone has been most cooperative and a spirit of sacrifice of self-interest in behalf of the organization's welfare has been a predominant feature. Where differences have arisen, compromise and unity have been the end results. For this, I am very grateful. I personally have always tried to do whatever was best for our organization and if at times personal feelings had to be sacrificed, I feel everyone has had the realization that animosity and personalities were not determining factors.

The testing time is now at hand. New faces, younger men, new officers, new ideas, all are now to be put to use. The narrower confines of gastroenterology have been broken and a wider scope, which promises a greater possibility of coordinated effort in this field, is now possible. I am confident that the opportunities for a good future in gastroenterology have been enhanced by our new organization. We now are ready to welcome all competent and qualified men in this field to take part in our organization.

I confidently expect to see the American College of Gastroenterology develop into an organization which will be of great benefit to the members, as well as to the cause of gastroenterology. So, I wish to express my sincere thanks to all who have worked and sacrificed to make our College posible.

To our offcers who carry on during the coming year, I wish the same cooperation and help accorded me.

Sigurd W. Johnsen

EDITORIAL

To Smoke or Not to Smoke

Experimental data from peptic ulcer patients show significant increase in gastric acidity under certain test conditions. Smoking is not an etiologic factor in peptic ulcer. It may, however, make them worse.

The effect on the alimentary musculature shows inhibition of automatic movements which are later augmented as a result of first, stimulation and later, depression of the autonomic nervous system. The inhibitory state is almost coincident with the period of smoking and is associated with contraction of the pyloric and ileocolic valves. Stimulation of the sympathetic nerves causes inhibition of the whole alimentary canal with the exception of these two valves which are contracted. The mild laxative action of tobacco smoke may be explained by the ultimate depression of the inhibitory cells, whereby the motor nerves assume an undue influence on the automatic movements. In nicotine poisoning, overactivity of the intestine tend to produce diarrhea. X-ray studies show that smoking produces colonic hyperirritability which may express itself in either diarrhea or spastic constipation.

A further effect of smoking is the production of heartburn—symptoms imitating those of duodenal ulcer cardio- and pylorospasm. Suffice it to say that the stomach usually shows a primary rise in secretion and in motility, followed at a later period by a depression. Smoking also tends to inhibit hunger contractions, lessening appetite and for a time, may diminish the pangs of hunger.

Patients with functional gastric disturbances have reported the prompt appearance of hyperacidity and/or heartburn when they smoked on a fasting or empty stomach, and absence of acidity or heartburn when they abstained from smoking.

The commonest symptoms of excessive smoking are loss of appetite, chronic gastritis and chronic intestinal catarrh.

It is generally conceded that moderate smoking produces no apparent injury to healthy individuals with normal stomachs. Certain victims of ulcer are habitual smokers, they claim to derive pleasure and a sense of euphoria. Ulcer patients should be cautioned to moderate their smoking habits.

There is a slight suggestive evidence that excessive smoking with inhaling, by nursing mothers, may lessen the quantity of milk and hurt the infant. There is also some evidence that inhaling the smoke by prospective mothers may harm the unborn child. In pulmonary conditions, especially tuberculosis, asthma and chronic bronchiectasis, it is advisable to limit or abstain from smoking.

About seven years ago, studies were carried out on the effects of cigarette smoking on a group of male and female patients (96 in number) at the New York

Polyclinic Medical School and Hospital. These patients were carefully observed as to their smoking habits and various tests carried out to determine the effect of moderate and excessive cigarette smoking on digestion, acidity, secretion of saliva, secretion of mucus and bowel stimulation or retardation.

Some patients had no gastric complaints, others had ulcers, or complained of heartburn and/or indigestion, flatulence and fatigue. The conclusions arrived at were that smoking immediately or within 15 to 30 minutes after eating did not materially increase the hydrochloric or total acidity. In a number of patients (25), the saliva and the mucus secretion in the stomach was increased which undoubtedly lowered the acid value. These tests were carried out on a fasting stomach, after an Ewald meal, after 7 per cent alcohol, neutral red, 1:1000 histamine and a 1 per cent solution of pepsin injection.

Patients who persisted in smoking three-quarters or one hour after meals or were chain smokers who smoked before breakfast and at night, were not relieved from their heartburn, indigestion or ulcer symptoms.

Recent tests show that certain cigarettes with an adequate filter have less tendency to increase hyperchlorhydria.

SAMUEL WEISS, M.D.

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In Memoriam

We record with profound sorrow the passing of Dr. Arthur A. Sachs, Elmhurst, N. Y., Member, of the National Gastroenterological Association.

We extend our deepest sympathy to the bereaved family.

NEWS NOTES

Twelfth Annual Meeting American Psychosomatic Society

The American Psychosomatic Society will hold its Twelfth Annual Meeting at The Claridge Hotel in Atlantic City on Wednesday and Thursday, May 4 and 5, 1955. This Meeting will be immediately preceded by those of the American Society for Clinical Investigation and the Association of American Physicians. It will be followed by the meeting of the American Psychoanalytic Association.

The Program Committee would like to receive titles and abstracts of papers for consideration for the Program no later than December 1, 1954. The time allotted for the reading of each paper will be twenty minutes. The Committee is interested in investigations in the theory and practice of psychosomatic medicine as applied to adults and children in all of the medical specialties, and in contributions in psychophysiology and ecology.

Abstracts for the Program Committee's consideration should be submitted in duplicate, and should be sent to the Chairman at 551 Madison Avenue, New York 22, New York.

Pamin

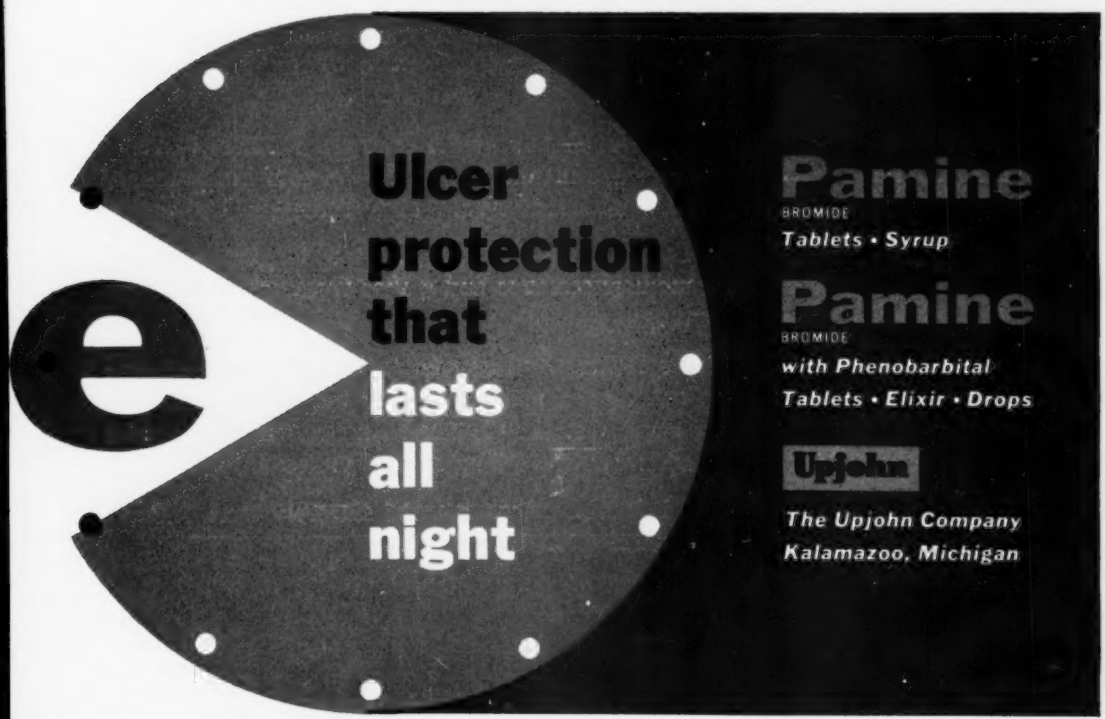
REGISTERED TRADEMARK FOR THE UPJOHN BRAND OF METHSCOPOLAMINE BROMIDE

Teaching Fellowship in Proctology

The International Academy of Proctology announces the establishment of a Teaching and Research Fellowship in proctology under the direction of Dr. Marcus D. Kogel, Dean of the newly formed Albert Einstein College of Medicine, New York City. The Academy has voted a $1,000 Annual Grant for each of three years to assist in the development of research and educational projects in proctology at the University.

One of the suggested projects is the establishment of a pathological tissue slide "library" for teaching purposes, under the direction of Dr. Alfred Angrist, Professor of Pathology.

The Academy offers a Teaching Seminar, open to all physicians without fee, each year. Research Fellowships in proctology are sponsored by the Academy, and three such Fellowships were voted at the time of the last Annual Meeting. Dr. Earl J. Halligan, Director of Surgery of the Jersey City Medical Center, and International Secretary-General of the Academy, is in charge of a Research Fellowship at the Jersey City Medical Center. Additional Fellowships were voted to be established in the Mid-west and on the West Coast of the United States.



College Secretary to Retire

It is with deep regret that we announce the retirement from active national medical politics of Dr. Ahbrohm Xerxes Rossien, upon the completion of his term of office as Secretary. The pressure of local medical commitments and his study of medical jurisprudence has necessitated this decision.

Dr. Rossien is one of the Charter and Life Fellows of the American College of Gastroenterology which he moved for and diligently pursued to its activation.

For the past three years, Dr. Rossien has served as Secretary of the National Gastroenterological Association and the American College of Gastroenterology. He is at present a member of the Editorial Council of our official publication, The American Journal of Gastroenterology, and was at various times a member of the Editorial Board, Editorial Council and Abstract Committee of its predecessor, the Review of Gastroenterology.

Dr. Rossien is an Assistant Clinical Professor of Medicine at the New York Medical College; Director of Post-Graduate Courses at the Medical Society of the County of Queens; Consultant Physician and Gastroenterologist at six major New York City and State hospitals; Attending Gastroenterologist at the Triboro Hospital of the Queens General Medical Center; Chief of Gastrointestinal Clinics and Gastroenterologist-at-large at the Jamaica Hospital. He is the author of some 50 articles on various phases of gastroenterology and research. In 1945, Dr. Rossien was the recipient of a citation for "outstanding and distinguished services" from the Commissioner of Hospitals of New York City.

Dr. Rossien received his medical degree at the Jefferson Medical College, in Philadelphia, in 1925 and continued his medical studies at four Postgraduate schools including the University of Pennsylvania and Columbia University.

In addition to being a Fellow of the American College of Gastroenterology, he is a Fellow of many other medical societies and a Vice-President of the New York Academy of Gastroenterology.

Dr. Rossien has often expressed his firm conviction that "To be a sincere physician one *must not only* be steeped in and practice the sound principles of democracy but *must also* carry God in his heart and not merely render Him lip-service" His civic contributions are too many to enumerate.

We wish Dr. Rossien well in all his endeavors and sincerely trust that we will have the benefit of his counsel from time to time.

ABSTRACTS FOR GASTROENTEROLOGISTS

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INTESTINES

NEWER THERAPEUTIC METHODS IN ULCERATIVE COLITIS: A. Staehelin. Schweiz. med. Wchnschr., 83:883, (Sept. 19), 1953.

The European author expresses his views about the treatment of ulcerative colitis. In the acute febrile stage the tendency of the disease to spontaneous remissions makes evaluation of any therapy difficult. The treatment consists of bed rest, transfusions, water, electrolyte and vitamin replacements and Dermatol enemas. The dietary problem is not solved by a low residue diet because many patients do not tolerate milk or sugar. Therefore, the food selection must be individualized with particular emphasis on a high caloric, high protein intake. There is as yet no ideal solution of the problem of hypoproteinemia. Machella's method with protolysates and dextrimaltose feedings helps some cases and aggravates others. Chemotherapy and antibiotics should be considered a useful supporting therapy. ACTH and cortisone are dangerous because they increase the tendency to perforation of the bowel, a complication which was the main cause of death in this series even without such treatment. Psychotherapy has some beneficial effect in chronic cases but seems out of place in acute, highly toxic, febrile patients. Surgery is opposed in acute ulcerative colitis without complications because the mortality of colectomy under such circumstances is not different from that of medical treatment. Surgical intervention is indicated in chronic cases for intractability as well as for various complications.

H. B. EISENSTADT

THE TREATMENT OF AMEBIASIS: R. Crosnier. La presse medicale, 61:1199, (Sept. 23), 1953.

The treatment of amebiasis must be of long duration as it is a chronic recurrent disease. The subsidence of acute symptomatology is less important than the sterilization of the intestinal tract. A recent infection with amebiasis should be curable within six months provided that the treatment is continuous and the patient is protected against reinfection.

The acute phase is treated with Conessine (alkaloid from bark of indian conessi tree or emetine for ten days with Terramycin (2 gm. daily) added. This treatment is followed by Iodoquin or Stovarsol together with Vitamin B (yeast) and lactic acid preparations for three weeks. The latter "consolidation treatment" is given 3 to 4 times a year for the next 2 years.

Chronic cases of amebiasis get a similar routine but without the therapy used for acute attacks.

Hepatic amebiasis must also be treated for a long time as a recurrence of the hepatitis is possible. Emetine, conessine, Chloroquine, and Terramycin might be required for this complication. In addition a proper diet for enterocolitis should be used. Sulfonamides might have to be added for bacterial superinfections.

H. B. EISENSTADT

TWENTY-EIGHT CASES OF TAENIA SAGINATA TREATED WITH THE MIXTURE OF HEXYLRESORCINOL AND TETRACHLOROETHYLENE: Jose G. Basneuvo and Francisco Soler. Arch. med. de Cuba, 4:625, (Nov.), 1953.

A mixture of hexylresorcinol and tetrachloroethylene was given either in capsule form orally or in liquid form transduodenally for the treatment of tape worm. The capsules contain Rx hexylresorcinol 0.05 gm., tetrachloroethylene 0.2 c.c., chenopodium oil 0.025 c.c., peanut oil to make 0.6 c.c. per capsule. Adults are given 20 capsules in the fasting condition, children 1 capsule per year of weight. Five capsules were taken every 10 minutes with a little sugar water in the morning. Transduodenal liquid had the following composition: Rx hexylresorcinol 1 gram, tetrachloroethylene 4 c.c., peanut oil q.s. 15 c.c. S. give entire amount mixed with 30 c.c. of syrup or 30 per cent acacia solution. On the day preceding treatment, only a light diet and a saline laxative in the evening were given. On the day of therapy, the patient remained fasting until four hours after the administration of the medication. At this time, liquids were taken and after four more hours, soft food. In the evening of this day the saline laxative was repeated. Cure rate by this method was 89 per cent.

H. B. EISENSTADT

THE SPRUE SYNDROME SECONDARY TO LYMPHOMA OF THE SMALL BOWEL: Marvin H. Sleisenger. Am. J. Med., 15:666, (Nov.), 1953.

Intestinal lymphoblastomas may produce a typical sprue syndrome with diarrhea, steatorrhea, sore tongue, weight loss, clubbing of fingers and toes and protein, vitamin and electrolyte deficiency indistinguishable from primary sprue. X-ray may also show only a deficiency pattern. A conservative sprue treatment with high caloric, high protein and carbohydrate and low fat diet, liver extract vitamins, minerals, etc., will temporarily benefit the patient and might achieve considerable weight gain.

Suspicion of secondary sprue might be aroused by the recent onset of the disease in contrast to primary sprue which is frequently present for years by the time the patient presents himself for clinical examination. Otherwise, the appearance of an abdominal mass, an intestinal obstruction, perforation or hemorrhage, an organic bowel deformation on the x-ray picture, a lymphadenopathy or a lymphoma of the skin and other organs may lead to the correct diagnosis.

H. B. EISENSTADT

ORAL USE OF HYDROCORTISONE IN TREATMENT OF SPRUE: David Adlersberg. A.M.A. Arch. Int. Med., 92:612, (Nov.), 1953.

A group of patients with intractable sprue, previously successfully treated with ACTH and Cortisone, were put on oral hydrocortisone in free alcohol form and hydrocortisone acetate. While hydrocortisone free alcohol proved to be just as effective as ACTH and Cortisone in controlling the symptomatology, hydrocortisone acetate was ineffective. The initial total daily amount of hydrocortisone free alcohol was 80 mg. This was divided in 2-4 equal doses. For maintenance, only 20-30 mg. were required once daily, best administered one half-hour before breakfast. This dose had to be increased in times of stress, especially during intercurrent infections and emotional upsets. The steroid improved inappetence, malaise, weakness, diarrhea, steatorrhea and deficient vitamin and mineral absorption. A significant improvement of x-ray changes was only occasionally observed. The clinical remission lasted only as long as the drug was taken. Therefore, the treatment had to be continuous. Side-effects were much less with hydrocortisone than with ACTH and Cortisone.

H. B. EISENSTADT

ULCERATIVE COLITIS (The Psychoanalyses of Two Cases): A. Karush and G. Daniels. Psychosomatic Med., 15:140-167, 1953.

This report concerns two female patients. Before becoming overtly ill, both women have struggled since early childhood with anxiety and rage. They were prevented from venting these emotions by fear of retaliation which took the form of fear of

mutilation and death. Finally, all mature adaptation failed with a regression to state of exaggerated dependency. The desired dependency being frustrated, resulting in depressive reactions. The trigger for the attacks was any threat to their security. Because of their inability to master any frustration, there was a lack of stability (disturbance of homeostasis). One patient was able to give some expression to her anger which was accompanied by constipation. Her rage was soon followed by depression, anxiety and diarrhea. It is felt that psychoanalytical investigation cannot resolve the "enigma of organ selectivity". It is possible, in the authors' views, that infantile fears may be alleviated so that the patient becomes conditioned to future tensions.

REGINALD B. WEILER

BACTERIAL FOOD POISONING: Liz Moser. Deutsche Med. Wchnschr., 78:1762, (Dec. 18), 1953.

Bacterial food poisoning, especially mass poisoning, is more frequently caused by nonpathogenic germs than by specific intestinal pathogens (shigella, salmonella). Among the nonpathogenic bacteria a special strain of staphylococcus producing enterotoxin is the most common offender. It propagates chiefly in milk, ice cream, boiled ham and pastry kept without refrigeration. The toxin causes an alarming attack of vomiting and diarrhea with shock, but the mortality of the disease is low. The presence of staphylococci in the suspected food is insufficient evidence of food poisoning, however, subcutaneous injections of a bacterial free filtrate from a broth culture of these staphylococci will produce an identical gastroenteritis in animals. Contamination of food with these staphylococci is due to handling by persons with suppurative lesions. The other group of nonpathogenic bacteria causing food poisoning includes *escherichia coli, proteus vulgars,* and *anerobic clostridia.* They exert their toxicity by means of nonspecific substances of protein putrefaction. The clinical picture of this disease is frequently less fulminating but its mortality is higher. Only an abundance of these nonpathogenic germs are able to produce enough poison to make clinical symptoms. Therefore, the suspected food must contain them in masses. Boiling does not destroy staphylococcic enterotoxin, the substances of protein decomposition, and the spores of anaerobes. Cleanliness and health of food handlers and proper refrigeration of food are the best means of prevention of food poisoning.

H. B. EISENSTADT

SUCCESSFUL TREATMENT OF INTESTINAL MONILIASIS WITH FATTY ACID RESIN COMPLEX: Irene Neuhauser. A.M.A. Arch. Int. Med., 93:53-60, 1954.

Three patients with extensive intestinal moniliasis, one spontaneous and two after use of wide spectrum antibiotics were apparently cured by the oral administration of an acid absorbing resin attached to a fatty acid, especially undecylenic or caprylic acid. The latter was the most effective. Dosage of this drug was four grams daily divided in four equal doses of four 250 mg. capsules. Such unions of anion exchange resins with acid drugs undergo slow hydrolysis in the intestinal tract assuring a uniform distribution of fine particles of the antimycotic fatty acids. Further investigation of such substances is needed in view of the increasing number of gastrointestinal fungus infections.

H. B. EISENSTADT

LOCAL HYDROCORTISONE ACETATE FOR RADIATION PROCTITIS: A. Hurtig. Postgraduate Med., 15:37-39, (Jan.), 1954.

Four cases of radiation proctitis, complications of radiation of the *cervix uteri,* treated successfully with local hydrocortisone acetate are described. Radiation proctitis and sigmoiditis occur in some 10 to 20 per cent of patients radiated for carcinoma of the female sex organs.

The medication is instilled through a rubber catheter followed by normal saline solution. Relief was immediate but Aureomycin by mouth was given to aid in overcoming infection. Radiation cystitis may be similarly treated.

REGINALD B. WEILER

GANGRENOUS BOWEL; CURRENT THERAPEUTIC CONCEPTS: C. P. Schlicke. Postgraduate Med. 15:5-10 (Jan. 1954).

The viability of the bowel in intestinal obstruction is the prime consideration. Any case of abdominal pain must be suspected as having an intestinal obstruction, and the possibility that strangulation is the cause must never be overlooked. Essential therapy includes treatment of shock with correction of fluid and electrolytic balances. Intubation should aim at emptying the stomach and if some flatus can be withdrawn from further down that is well but prolonged attempts at passage should be avoided. Surgery is the prime indication so that the gangrenous segment should be removed as early as feasible so that intestinal continuity is reestablished. All other measures should be used according to indication but it must be recognized that surgery is the only curative and life-saving measure.

REGINALD B. WEILER

LIVER AND BILIARY TRACT

CHOLECYSTO-CHOLANGIOGRAPHY WITH BILIGRAFIN: L. Niemgeers and J. Maerman. Acta Gastro. Belgica 17:38, (Jan.), 1954.

The authors report 25 nonselected cases of cholecystocholangiography with biligrafin. No visualization at all, in two cases; in two other cases the gallbladder was excluded by the peroral method. A very good cholangiocholecystography was obtained by the new drug. A good cholecystocholangiography was obtained in 22 out of 25 cases (88 per cent). Perfect visualization was performed in all five cholecystectomised patients. These numbers correspond to Hagedorn's statistics. The biggest advantage of the new drug is the short visualization time, (time between the administration and the visualization of the bile ducts) and darker contrast of the cholangiography films, even after cholecystectomy.

FRANZ J. LUST

Pamin

REGISTERED TRADEMARK FOR THE UPJOHN BRAND OF METHSCOPOLAMINE BROMIDE

AN EVALUATION OF SOLUTIONS FOR FRAGMENTATION AND DISSOLUTION OF GALLSTONES AND THEIR EFFECT ON LIVER AND DUCTAL TISSUE: R. R. Best, J. A. Rasmussen, C. E. Wilson, Ann. Surg., 138:570 (Oct.), 1953.

The incidence of stones remaining in the common duct following cholecystectomy and choledochostomy remains an interesting and perplexing problem. Nonoperative management of retained calculi is presented with three approaches in mind. (1) Physiologic flush with hydrocholeretic; (2) Chemicals for the solvent and fragmentation action on stones; (3) Sphincter anesthetics and relaxants. One hundred thirteen different chemicals alone and in combination with chloroform or ethyl ether were tested for effect on stones and their toxic action on liver and ductal tissue. Warm chloroform was found to be the best solvent with ethyl ether second best. A method is presented for fragmentation and dissolution of retained biliary tract calculi emphasizing a three-day "biliary flush" regimen, combined with the use of both warm chloroform and ethyl ether instilled through a double lumen T tube with frequent check on results by choledochography.

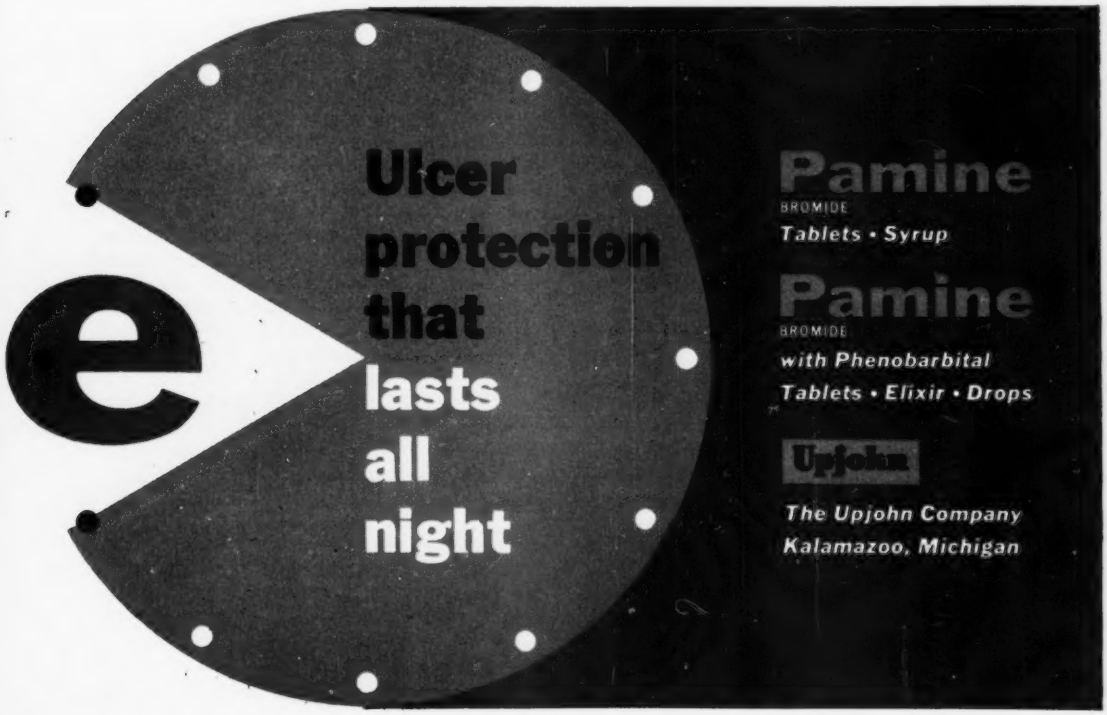
WILLIAM E. JONES

GALACTOSE FUNCTION TEST SENSIBILIZED BY PRIOR HISTAMIN INJECTION: P. Leonard. Acta Gastro. Belgica 17:27, (Jan.), 1954.

The galactose tolerance test after histamine injection, in the author's opinion, is able 1) to demonstrate the role of the liver in allergy: an important reduction of the galactose excretion is related to an exaltation of the hepatic cell. 2) to discover reactional jaundices or latent hepatitis.

Histamine appears to act essentially by dilatating the hepatic blood vessels, thus affecting the reactive power of the hepatic cell.

FRANZ J. LUST



AMEBIC HEPATITIS PRESENTING AS FEVER OF UNKNOWN ORIGIN: P. Heller, R. J. Koon, H. J. Zimmerman, New England J. Med., 29:596 (Oct. 8), 1953.

The authors present two cases of low grade fever that presented elusive diagnostic problems. Both patients eventually had symptoms and signs pointing to hepatic involvement and needle biopsies in both revealed focal necrosis. Complement fixation tests for amebiasis were strongly positive in both. Only one of the two patients can be said to have had proven amebiasis since in only one was E. histolytica in any form actually demonstrated. The authors state, "contrary to what may be expected in a presumably diffuse hepatitis, liver function and biopsy studies are of little specific significance in amebic hepatitis." In accepting a concept of diffuse hepatitis in amebiasis it would seem logical to accept the pathogenic concept applicable to solitary abscess formation; that is the theory of "amebic" emboli progressing from the colon to the liver via the portal circulation. Such multiple emboli would produce a diffuse focal hepatitis and probably be accompanied by normal liver function studies. Such were the findings in the authors cases.

WILLIAM E. JONES

CHRONIC CHOLECYSTITIS AND ROKITANSKY ASCHOFF SINUSES: H. Lapointe. J. Canad A. Radiol. 4:45-46, (June), 1953.

The visualization of Rokitansky-Aschoff sinuses during cholecystography is quite a rare occurrence; the condition usually being found by the pathologist. The sinuses are hernia-like protrusions of the mucosa through the muscular layer of the gallbladder and are actually intramural diverticula.

At the Mayo Clinic a study of 405 gallbladders demonstrated that 93 per cent of the chronically inflamed gallbladders had diverticula and that it was exceptionally found before the age of 30.

In the case reported, the sinuses were easily visible on the five-hour film and had the appearance of a chain of pearl-like shadows around the contour of the gallbladder lumen. Why it is that only seven cases have been reported in the literature when it is so common pathologically, may be due to the small size of the sinus orifices, the thickness of bile, lack of five-hour films, failure to give a fat meal, and failure to use the oblique position.

J. R. VAN DYNE

THERAPY OF ASCITES IN PATIENTS WITH CIRRHOSIS OF THE LIVER: Editorial—Arthur L. Bloomfield. A.M.A. Arch. Int. Med., 92:603, (Nov.), 1953.

Therapy of ascites has to consider at least five factors influencing ascites formation: portal hypertension, abnormal vascular permeability, antidiuretic hormones, inability of the renal mechanism to excrete sodium, and low oncotic pressure due to hypoproteinemia. These five factors contribute in different degrees to each case of ascites, therefore, treatment must be individualized. Extreme restriction of salt intake together with salt elimination by paracentesis, mercurial diuretics, resins, etc., is helpful only in a certain number of cases, while others develop electrolyte derangement with low serum sodium and chloride and high serum potassium. The danger of electrolyte disturbance is especially great when ascites returns rapidly after an initial paracentesis in spite of a low salt diet. Under such circumstances one should abandon the sodium restriction and attempt to influence the other factors as ascites formation.

H. B. EISENSTADT

PORTAL CIRRHOSIS, CORRELATION BETWEEN THE SEVERITY OF ESOPHAGEAL VARICES AND VARIATIONS IN PHYSICAL FINDINGS: E. D. Palmer, and I. B. Brick, Am. J. M. Sc. pp. 149-151, (Feb.), 1954.

As a result of series of esophagoscopic evaluation of varices in 60 cirrhotic patients, and the comparison with changes in the clinical signs of portal hypertension, the authors conclude that there is no constant direct or reciprocal relationship between varix severity and hepatomegaly, splenomegaly and ascites. The state of esophageal varices cannot be estimated from changes in physical findings. Esophageal varices may appear and disappear under the conditions of a static clinical picture. Whatever the various relationships may be, sudden alterations in the severity of esophageal varices

must be recognized if proper use is to be made of surgical decompression technics. It is clear that the clinician cannot rely on physical signs to help in evaluating varix severity.

J. R. VAN DYNE

PANCREAS

CHOLEDOCHOENTEROSTOMY IN CHRONIC RELAPSING PANCREATITIS: L. M. Rousselot, R. Sanchez-Ubeda and S. Grannelli. New England J. Med. pp. 267-272, (Feb. 18), 1954.

Five cases of chronic relapsing pancreatitis treated by choledochojejunostomy are reported with only one good result (in this case cholecystectomy for previously undiagnosed cholesterosis accompanied the procedure). To the best of the authors' knowledge this is the first negative report supported by documentary clinical evidence, and long follow-up period.

Criteria for the diagnosis of chronic relapsing pancreatitis are presented. The failure of operations dividing biliary and pancreatic flows is considered suggestive evidence against the common channel theory of pancreatitis operating in all cases of pancreatitis.

J. R. VAN DYNE

CHRONIC PANCREATITIS-PATHOGENESIS AND CLINICAL FEATURES: Arthur M. Phillips. Arch. Int. Med. 93:337, (March), 1954.

Chronic recurrent pancreatitis is not an uncommon disorder according to the observation of the author. This disease should be considered in males giving a history of spells of indigestion for a period of many years at the rate of once to a few times a year. The patients are usually chronic alcoholics with personality disorders responsible for the alcoholism. Because of a psychoneurotic or psychotic makeup, the digestive disturbances are attributed to nervousness. The spells follow mostly the intake of alcohol, the amount of which might be small, especially if the disease is of long standing. The episodes are characterized by severe upper abdominal pains which might radiate to the back or to either shoulder, by nausea, vomiting and diarrhea. The latter symptoms subside rapidly as soon as the pain ends. Hematemesis might occur due to associated gastritis or peptic ulceration. Creatorrhea, steatorrhea and diabetes are found only in 30 per cent of the cases. Transient liver dysfunction with or without jaundice may be noticeable during the attack. The gallbladder might fail to be visualized temporarily with cholecystography even in the absence of gallbladder pathology. Complications of recurrent pancreatitis are pseudocysts, peripancreatic hematoma, pancreatic and subphrenic abcesses. Gallbladder or liver disease are usually considered to be causative factors of recurrent pancreatitis but are more often sequelae of primary pancreatic disease in the author's experience. The acute flare-up of chronic pancreatitis is best treated conservatively while the sequelae require surgical therapy. In addition, various surgical methods as sympathectomy, vagotomy, sphincterectomy and pancreatectomy have been tried to alleviate the recurrent pains. The success of these procedures, however, is uncertain because of the underlying psychoneurosis with alcoholism.

H. B. EISENSTADT

DOES THE SPHINCTER OF WIRSUNG'S CANAL PLAY A PART IN THE PATHOLOGY OF THE PANCREAS ANATOMICAL AND RADIOLOGICAL DATA? Lucien Leger and Jacques Lataste. Presse Medicale, 62: No. 14, 1954.

The tendency of giving a larger place to Wirsung's canal in pancreatic pathology, the supposed role of this canal in the biliopancreatic reflux, the possible presence of a syndrome from dystonia of the pancreatic sphincter, have prompted the authors to resume an anatomoradiologic study of this sphincter, as classical text-books give little information in regard to its situation and even to its real presence.

From this anatomoradiologic study it appears that the true pancreatic sphincter, as physiologically considered is constituted by the upper portion of Oddi's sphincter. Those muscular fibres, situated around Wirsung's canal just before its junction with the choledochus, are inconstant and incompletely circular, so they do not seem able to play

an efficient sphincteral role. The importance of the reflux into Wirsung's canal as visualized during cholangiography appears to be less relevant to the tonicity of the pancreatic sphincter than to the balance between the pressure in the Wirsung's canal and the choledochus on one hand and the miscibility of the contrast fluid and pancreatic juice on the other hand.

The sphincter of Wirsung's canal, being considered its minor significance, appears to play only a limited and possibly inconstant role in the pathology of the pancreatic gland.

GUY ALBOT

REBOUND OF PANCREATIC DISEASES OF THE SPLEEN: Lucien Leger, Paul Lajouanine, Andre Cornet and Jacques Arnavielhe. Presse Medicale, 62: No. 31, 1954.

The close connection of the splenic vein with the body of the pancreas accounts for the rebound of this gland's diseases on its satellite vessel and the spleen. With the use of splenoportography it is possible to show this morphologic repercussion and to explain a certain number of functional changes (splenomegaly, hemorrhages) which have hitherto received little attention.

The authors present a first seres of cases concerning those carcinomas of the pancreas with posterior extension causing a compression or a thrombosis of the splenic vein and at times wrongly suggestive of the possibility for the splenomegaly to be primary.

In a second series of cases the portal hypertension located in the splenomesenteric system is caused by a pressure on the splenic vein from a lesion of the pancreas body which can induce a digestive hemorrhage. Such facts were not ignored but they were inadequately explained. Now with splenoportography it is made possible to afford the desired pathogenetic explanation.

This method of exploration seems greatly informative in the cases of digestive hemorrhages and should be routinely performed.

In addition, there are some clinical pictures of Banti's syndrome type for which an initial explanation might be found in a pancreatic lesion.

Splenoportography allows a better estimation of the "operability" of pancreatic tumors, that is to say whether one should give up any idea of surgical exeresis or, on the contrary, extend the exeresis as far as the vena porta which sacrifice is now recognized to be possible.

GUY ALBOT

PATHOLOGY AND LABORATORY RESEARCH

MORPHOLOGIC STUDY OF THE MYENTERIC PLEXES AND MASCULATURE OF THE PYLORUS WITH SPECIAL REFERENCE TO THE CHANGES IN HYPERTROPIC PYLORIC STENOSIS: H. H. Belding, 3rd; J. W. Kernohan. Surg. Gynec. & Obst., pp. 323-334 (Sept.), 1953.

In this study the ganglion cells and nerve fibers of the myenteric plexus and the musculature of normal stomachs and duodenums and also of those affected by hypertrophic pyloric stenosis were investigated. In the stomach, pylorus, and duodenum of infants and adults who had hypertrophic pyloric stenosis, the following was found: 1. The number of myenteric ganglion cells and nerve fiber tracts per unit area appears to be reduced in the pyloric region but remains quantitatively normal or slightly increased in the stomach just below the incisura and in the duodenum. 2. The circular muscle of the pylorus of both infants and adults is two to four times as thick as that of normal infants. 3. The most significant and constant findings in this study was that the majority of myenteric ganglion cells in the pylorus show degenerative changes resembling those seen after excessive vagus nerve stimulation. Such changes are not seen in the myenteric ganglion cells in the stomach above the pylorus nor in the duodenum in pyloric stenosis or in normal individuals. These changes should be sharply contrasted with the congenital absence of myenteric ganglion cells found in the so-called stenosed area in congenital megacolon.

The following observations were also found: 1. Segments of longitudinal muscle are often found to be absent in the pylorus of normal infants as well as of those infants who have hypertrophic pyloric stenosis. 2. There is a definite fibrous block between the circular musculature of the pylorus and that of the duodenum while the longitudinal muscle is continuous in the two segments. 3. These findings seem to lend support to the neurogenic theory of the etiology of hypertrophic pyloric stenosis.

J. R. VAN DYNE

EXPERIMENTAL EXIT ULCER: C. Debray and J. P. Hardouin. Arch. Mal. App. Digestif. 42:452-501, (April), 1953.

The experimental exit ulcer is the one which forms at the point where, immediately below the stomach, the gastric secretions strike the small intestine. It results from the disequilibrium produced between the attacking hydrochloric-peptic juice and the defense set up by the duodenopancreaticobiliary secretions and by the resistance of the wall.

Certain ulcers are clearly connected with the fragility of the wall of the intestine, whose mucous membrane, becoming increasingly less resistant as it gets further away from the stomach, will be digested by the gastric juice. The ulcer of Meckel's diverticulum is a good example of really spontaneous formation in man. It is situated on the mucous membrane of the small intestine, just at the exit of the diverticulum whose mucous membrane has undergone gastric heterotopia. Since 1932 Matthews and Dragstedt have been able to reproduce this ulcer experimentally.

The suppression of the buffer value of the pancreaticoduodeno-biliary secretions also invites an experimental exit ulcer. The supression of the biliary secretion, especially if there is at the same time retention, as in the simple ligature of the choledoch arouses particular susceptibility to ulcer. The pancreatic juice plays a role, but it is a less important one.

In order to increase the volume, the duration and the acidity of the secretion, the fictitious meal method was at first tried, but results were very unequal except where the general health of the animal was impaired. On the other hand, the injection of delayed-action histamine regularly provoked gastroduodenal ulcers either by gastric hypersecretion or by vascular disorders. Acute duodenal ulcers, set up by instilling hydrochloric acid into the stomach, have revealed several important facts: the importance of the permanence of the attack, the role of pepsin and various general factors such as acidosis and denutrition as facilitating factors.

Surgical experimental exit ulcers (Mann and Williamson's ulcer, ulcer after gastroenterostomy) are well known to experimenters and to surgeons: if the presence of the gastric juice is indispensable for their appearance, several factors, analyzed in this report, facilitate it.

The following are the report's main conclusions:

1. In experimental exit ulcer the presence of active hydrochloric-peptic juice is necessary. If this juice is deficient, the ulcer is not produced even in the combined presence of other experimental factors.

2. In most cases, various factors favoring it should be added. Amongst these should be noted the presence of pepsin, the absence of pancreatic and especially biliary secretions, acidosis, denutrition, the existence of slight parietal lesions.

3. Experimental exit ulcer and postoperative ulcer in man are almost identical. On the other hand, and despite disturbing similarities, it is not possible to identify experimental exit ulcer exactly with spontaneous duodenal ulcer in man.

FRANZ J. LUST

NUTRITIONAL STANDARDS, ORGANIZATION AND MANAGEMENT OF SUMMER CAMPS FOR DIABETIC CHILDREN: Harry G. Jacobi. J. Clin. Nutrition. 1:384. (July-August), 1953.

Complete integration and cooperation of the medical and physical activities program is necessary for successful operation of camps for diabetic children. Food allowances of most of the campers were arranged under five basic diets which aided materially in the actual serving of the food to a large group of children. The success of such a camp program depends upon careful preliminary screening of applicants to decide on dietary intake and insulin dosage. All usual insulin dosage is routinely reduced by approximately 30 per cent for the first 24 to 48 hours of the camp stay. A well-arranged program of camp activities allowing for sufficient freedom of choice by the individual camper has been found to be most successful. Cost analysis of daily food consumption at camp per child showed it to be $1.17. Psychological evaluation studies were attempted for the first time on these children, with rather encouraging results.

FRANZ J. LUST

EXPERIMENTAL INGESTION OF SALMONELLA (EBERTHELLA) TYPHOSA: P. Noak, Harefuah. J. Israeli M. A. 45:247-248, (Dec. 15), 1953.

The author ingested a suspension of 500,000 virulent typhoid bacilli in 100 c.c. of milk to disprove the accepted view that typhoid may be contracted by ingestion of contaminated food. Organisms showed the same viability in a milk suspension as in a saline suspension, that is recovery after two hours but not after 18 hours. The author did not exhibit any clinical evidence of the disease and daily stool and blood cultures were negative. Though the original culture was Vi-positive, there was no increase in anti-Vi-agglutination titre in the author's serum. The experiment does not disprove the oral route of infection in typhoid, but does cast some doubt on its importance.

ARNOLD L. BERGER

PSYCHOSOMATIC MEDICINE

PSYCHOANALYSIS AND MORAL DEVELOPMENT: H. G. Van der Waals, Ned. Tijdschr. Psychol., 6:73-90, 1951.

It is not fact that psychoanalysis regards all guilt feelings as neurotic. Psychoanalysis recognizes that the development of the conscience is a difficult and complex process. In abnormal development conscience may become a danger instead of a safeguard. The formation of a social sense necessitates a predominance of subjective responsibility over objective desires. Psychoanalysis has demonstrated the important part played by fear, aggression and love in the development of a social conscience. Good moral development, in which love, rather than fear or aggression, occupies the important place serves to demonstrate that Christian principles and psychoanalytical findings point in the same direction rather than being opposed to each other. Psychoanalytical therapy seeks to free the individual from compulsory morality and substitute an autonomy in which the individual himself chooses and decides issues.

REGINALD B. WEILER

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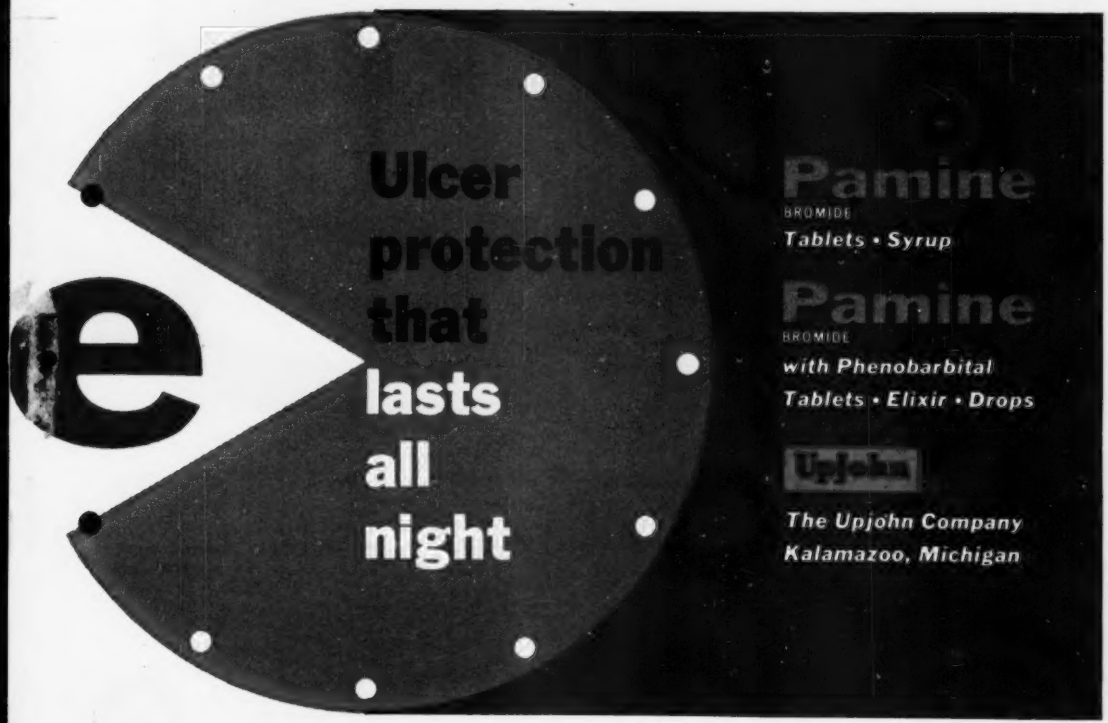
PSYCHOLOGIC IMPLICATIONS OF CANCER: Joost A. M. Meerloo. Geriatrics., 9:154-156, (April), 1954.

A survey of emotional aspects of malignancy will serve to reveal the subtle and paradoxical results of fear and prejudice as well as provide new clues in the study of malignant growths. Problems involve: 1) the subjective attitude of the patient, family, physician and others in contact with the patient; 2) Special emotional significance of the affected organ; and 3) Specific psychosomatic concepts of cancer including cancer phobia, refusal to recognize the disease, and unwillingness to accept help.

The following may be suppositions to be explored: 1) Emotional and somatic effects may stem from a common cause; 2) Psychological reactions may be secondary; 3) A similar etiology for both; 4) The emotional disorder may be first sign of malignancy; 5) A common factor may result in both processes; 6) An unconscious emotional factor may be definitive in selection of particular organ site of cancer; 7) Cancer phobia may result from over stress in publicity campaigns; 8) Stress, trauma (mental), or maladaptation may be causative factors in malignancy; 9) Emotional factors may be active in producing environmental celular factors favorable for malignant degeneration; 10) Investigators in cancer research may unconsciously shy away from consideration of psychological factors; 11) Incurable cancer patients always require emotional support; there may be some undiscovered clue in such cases of malignancy which undergo spontaneous regression.

The author pleads for more objective consideration of emotions in cancer problems and stresses the need for a psychological orientation of physicians treating malignant patients. The possibility of emotional etiology is not beyond possibility.

REGINALD B. WEILER



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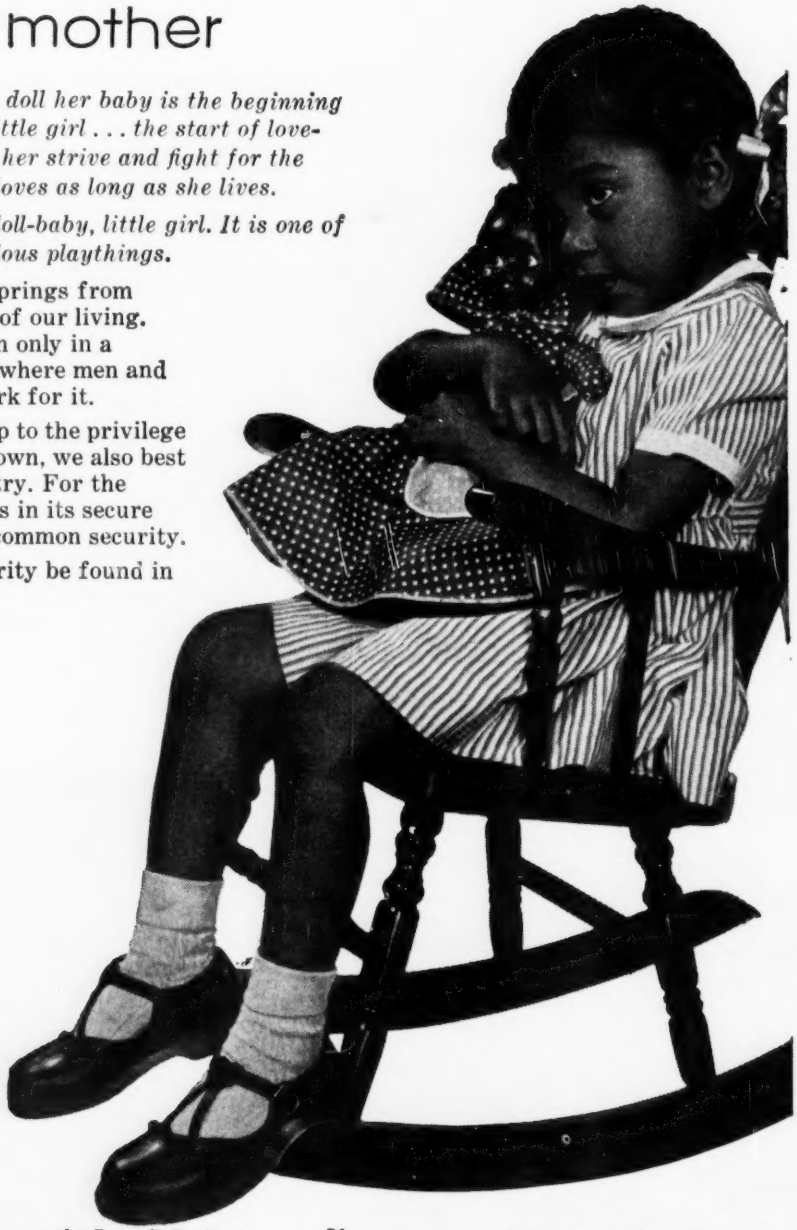

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1. ROGERS, W.P., AND GRAY, C.L.: AM. J. DIGEST. DIS. 19:180 (JUNE) 1952.

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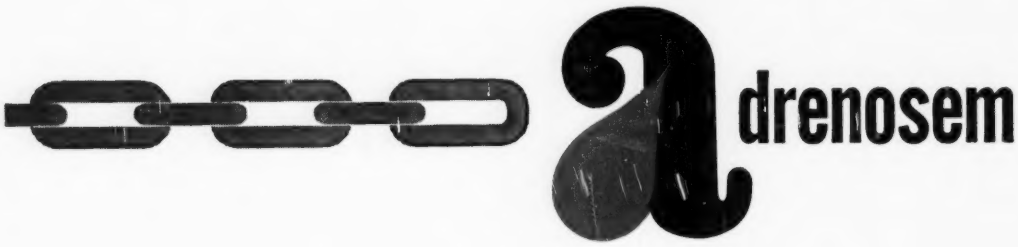
*Sherber, D. A.: The Control of Bleeding, Am. J. Surg. *86*:331 (Sept.) 1953.



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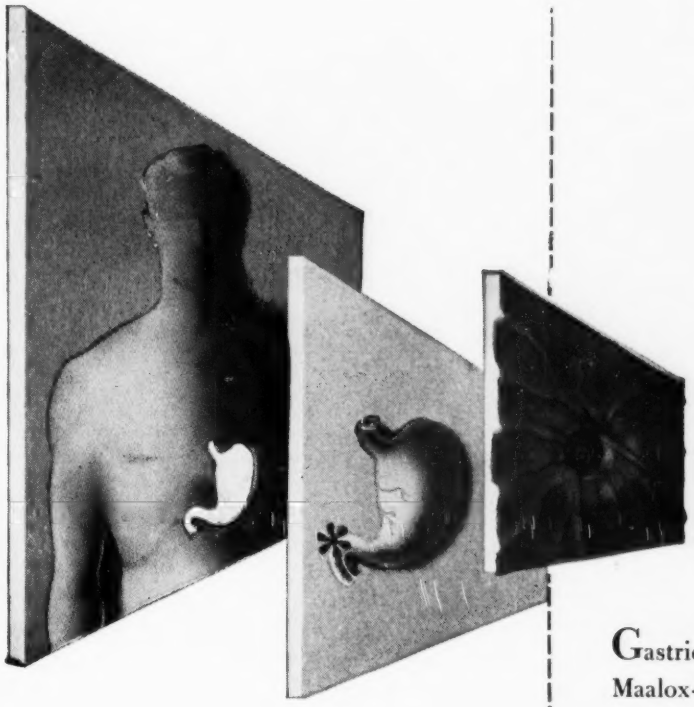

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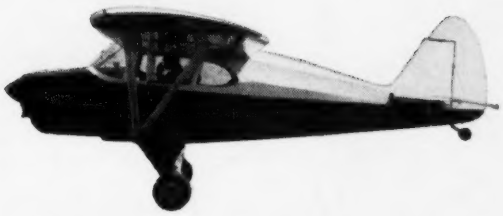

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